Digitized by the Internet Archive
in 2018 with funding from
University of Toronto

https://archive.org/details/medjournalJan1950uoft

THE UNIVERSITY OF TORONTO
MEDICAL JOURNAL

VOLUME XXVII TORONTO, JANUARY, 1950 NUMBER 4

THE BASIS OF SPECIFIC THERAPY

K. J. R. WIGHTMAN, M.D., F.R.C.P. (C), F.A.C.P.*

IT IS SURPRISING how little we know about the agents we use in treatment. We have learned a good deal about what drugs can do in the way of affecting function, combating infection or even producing structural alterations in the body, but for the most part we have not the faintest idea how they do these things. However, some progress is being made. The side-lights which are thrown upon the problem by research in a number of fields can be gathered together with some profit, although it must be admitted that the illumination thus provided is not very great. The first steps in the reactions induced by some of these compounds have now been identified, and a principle established which may bring forth greater results in the future.

The beginning came with the chemotherapeutic drugs. These were compounds of known chemical composition which attacked infecting organisms more or less specifically within the body, without exerting much effect on the cells of the host. It was Ehrlich who first postulated that it would be possible to find such a substance; until that time it was well recognized that there were agents which were toxic to living organisms, but they did not differentiate between parasite and host; they fell into the group which was called 'protoplasmic poisons' and it was felt likely that protoplasm of different origins was likely to respond to any toxin in a more or less uniform manner. However, Ehrlich had demonstrated that different tissues in the body could be stained selectively by injected dyes, and he considered that if one could find a stain selective for the organism and make it toxic as well, the answer would be at hand. His interpretation of the antigen-antibody reactions which were being explored at the time was that the two compounds fitted together by virtue of some specific structural or chemical configuration, and he felt that there might well be 'chemoreceptors' within the cell which would have specific chemical affinities as well. His work on the therapy of protozoal infections seemed to support this idea, but the nature of the receptor and the type of reaction which went on was never identified. This meant that the search for the right compound for other types of infection had still to be conducted on the basis of trial and error.

It was in this manner that the sulphonamides were discovered, after many thousands of compounds had been tested. They proved to be less specific than the anti-protozoal agents, in that

*Associate in Medicine, University of Toronto.

they affected numerous types of bacteria, instead of one or two. The interesting thing about them was that they were much more effective in vivo than one would expect from their behaviour in the culture tube. In fact it was extremely easy to nullify their action in a culture, by adding peptones, or tissue extracts, or extracts of bacteria which did not ordinarily respond to sulphonamide therapy. Investigation of this fact finally led to the observation that para-amino benzoic acid was a specific antagonist of the sulphonamides, and furthermore, that a ratio of antagonism could be worked out which determined which would have the upper hand in a mixture, as it were. This suggested that some chemical interaction of a quantitative sort was involved. Since the two compounds did not react with each other, it seemed as though some sort of balance between them and a component of the cell was involved. The concept of competitive reactions between an enzyme and two substrate compounds had already been formulated, and in view of the marked similarity in chemical structure between para-amino benzoic acid and sulphanilamide, it seemed that this was the answer. In other words, there was an enzyme in bacteria which used para-amino benzoic acid as a substrate normally. However, sulphanilamide could also combine with this enzyme, but would not participate in the reaction the enzyme usually catalyzed. This blocked one chain of metabolism, and the effect on the organism as a whole would depend on how important that chain was to it. In some cases the organism synthesized its own para-amino benzoic acid, and was indifferent to the intruding sulphonamide; in others the synthetic processes were carried out without going through this particular phase, so these organisms were unaffected.

The technique which was used to establish this hypothesis deserves further study, because it has made many other contributions to our knowledge. It developed out of an investigation of the requirements of bacteria for growth. A few organisms will grow in a medium which contains only sugar, water, urea and salts. However, most organisms require the presence of some more complicated substance, or possibly a combination of them. The specific minimal requirements of different organisms were more or less characteristic. For instance it was found that some required nicotinic acid, others thiamine, and so forth. These compounds were called 'growth factors' because they were necessary for bacterial growth. There were other compounds which stimulated growth, though their absence did not prevent it; these were known as essential metabolites. A growth factor for one organism might be an essential metabolite for another; the compounds thus identified evidently indicated the stages at which synthesis began in that organism, or through which it passed. In this manner it was found that para-aminobenzoic acid was either a growth factor or essential metabolite for most of the organisms which were affected by sulphonamides.

The other striking thing was that many of these compounds were known to be vitamins, which is only another way of saying that they are essential metabolites in the animal world as well as the bacterial. As the work went on, new compounds were found which had a growth stimulating effect on bacteria, or acted as growth factors, and it was logical to test them for vitamin activity

as well. In this way many of the components of vitamin B were identified, the latest being folic acid and vitamin B^{12}.

The same technique can be used to measure fantastically small amounts of these substances. The measurement of folic acid in urine for example, depends upon obtaining the organism for which folic acid is a growth factor and putting it in a medium which contains everything it needs except folic acid. Then various dilutions of the urine are added to different tubes of the culture, after which they are incubated. The tubes will show, at the bottom end of the scale, no growth, and at the top a number of tubes showing maximal growth. Between these extremes there will be a zone in which a gradation of growth from tube to tube can be observed, and the folic acid content of the dilutions used in these tubes can be calculated by comparison with cultures grown under standard conditions with various known amounts of folic acid. This procedure is known as microbiological assay, and it enables one to measure concentrations of substances like vitamin B^{12} even when their actual chemical composition has not yet been established.

In view of the chemical similarity between sulphanilamide and para-aminobenzoic acid, it seemed likely that 'analogues' of some of the other growth factors might be prepared by some kind of modification, which would lead to a chemotherapeutic effect. This has been accomplished, but for various reasons the practical results have not been very gratifying. In the first place, there may be so much of the natural substrate in the tissue fluids that effective competition is not possible. In the second place, it must be realized that these competitors become involved in the tissue enzyme systems too, and since the growth factor is very likely to have a vitamin action with regard to the host, a toxic effect may be produced—in short, an acute vitamin deficiency. The only reason that a selective action is exerted against bacteria is that the particular chain of reactions which is broken is a good deal more essential to bacterial growth than it is to the functioning of the tissues. An application of this fact has come with the production of anti-folic acid substances. It was observed that folic acid seemed to aggravate the course of acute leukaemia in children, and that leukaemic leukocytes contained more folic acid than normal ones. It therefore appeared that these cells made greater use of folic acid than the normal ones, and that a folic acid antagonist might affect them more. Accordingly, the chemists were asked to synthesize chemical analogues of folic acid, and the bacteriologists asked to determine which of them had the greatest inhibitory effect on folic acid in cultures of organisms which required it as a growth factor. The compounds thus discovered (aminopterin, amethopterin, and others) were then tested with regard to toxicity, and finally given a clinical trial in acute leukaemia. The compounds produced remarkable remissions in a proportion of the patients treated, but no cures.

The study of inhibitors of various growth factors in bacteriological cultures—that is to say, the identification of substrate competitors—is being applied to many fields of metabolism, and is throwing some light on the function which the growth factor plays in the organism. A further complication, known as 'inhibition analysis', consists in balancing a growth factor and its

inhibitor in the medium, and then seeing what third compound, if any, will allow growth to occur again. For example, you might find that a bacterium which requires para-aminobenzoic acid (p.a.-b.a.) for growth, in a medum with both that substance and sulphanilamide present, may resume growth when folic acid is added. Since p.a.b.a. is one of the components of folic acid, it would appear likely that the organism was using it to synthesize folic acid. However, the results obtained by this method can be completely incomprehensible, and must be interpreted with care. The use to which this sort of information can be put depends on the fact that an enzyme system which exists in bacteria is fairly likely to turn up somewhere in the animal world, and the interactions of compounds thus demonstrated are likely to hold good. The same types of technique have been applied to tissue cultures with the hope of determining what enzyme reactions can be affected there.

In the meantime, the question which remains to be answered is "what determines this 'affinity' which an enzyme has in one degree for one substance, and in another degree for a similar substance?" That brings us into a realm of chemistry and physics which has to do with the actual size and shape of molecules. It is a matter of spatial configuration and electromotive forces which remind one of the analogy of the key and the lock. The substrate may be defined not in terms of its chemical formula, but rather with respect to the electron concentrations which exist at nodal points in the molecule; how far apart they are in Angstrom units, where they are in relationship to each other, and what is the configuration in space of the molecule which carries them. These are details with which we cannot afford to concern ourselves very much, but they suggest one possibility which is worth bearing in mind, namely that "electro-physical analogues" to substrate compounds may exist which would appear to be quite different in a chemical sense.

The relationship of all this to our topic is this; it would appear that any specific effect which a drug produces in an organ or in a tissue (be it therapeutic or toxic) is determined by its effects on the enzyme systems present there. Let us then consider the present knowledge of enzymes in tissues. In the first place, almost without exception, they have to be identified by the things they do, rather than by direct analysis, since their composition is unknown. It is evident that they fall into two groups; those which break substances down and release energy, and those which synthesize things, and require energy. They seem to work in relays, and the change which a single enzyme produces in a compound may be very slight, after which the compound may pass on to another. An enzyme system may be considered to consist of an enzyme, a co-factor, an anti-enzyme or inhibitor and an activator. The degree of functional activity of the system at any moment depends on the balance of all these, some of which will be seen to be opposing each other. It will be seen at once that a therapeutic agent might act by affecting any one of them. With respect to the enzyme, it may act as a substrate competitor, forming a complex with it which may be either reversible or irreversible. Or it may react with a portion of the enzyme, deforming it in a way which prevents it from functioning (by neutralizing one of the electron concentrations, for example). Or it

may compete with the enzyme for its substrate, combining with it in a way which blocks the usual reaction. With regard to the accessory factors, one can visualize it inhibiting an activator, or activating an inhibitor, or substituting itself for any one of them and re-inforcing its action, or combining several of these activities in a bewildering complexity of action which indicates that it may be some time before we know all that is to be known!

These are some of the ways in which a compound may act; what determines where it acts? This would appear to be concerned with the distribution of enzymes. It is evident that there is a group of enzymes which is common to almost all living tissue; interference with these leads to death, and it is in relationship to these that the so-called "protoplasmic poisons" have their action. However, there are others which may be peculiar to one tissue, and these are the ones which would seem to determine the activity of a drug on that tissue and not on others. We know that an enzyme like phosphatase has a very characteristic distribution in the body; certain metabolic functions are concentrated in the liver and the kidney, for example, and served by special enzymes, and the peculiar substances produced by the ductless glands would indicate a very special set of enzymes in each of them. It should be possible, then, to find out what enzymes are being affected by some of the drugs now in use. However, it may not help us much for a while. Stilboestrol, which has a stimulating effect on the tissue of the breast and portions of the genito-urinary tract, a carcinolytic effect on tumours of the breast and prostate, and a carcinogenic effect on the breast turns out, in terms of enzyme chemistry, to be a hydrogen acceptor, which competes with enzyme systems which transfer hydrogen. How illuminating! It is obvious that we will have to go deeper than that.

The other possibility which is being exploited is that a cell in mitosis may be interfered with on the basis of reactions which are going on at that particular time. Thus tumour tissue, which shows more mitotic activity than normal tissue, may be more or less selectively affected by an agent that acts in this way. Whether this activity is determined by enzymes, or whether it has to do with the reactivity of the nucleoproteins of the chromosomes is not yet established. So far, with the possible exception of the folic acid antagonists, it has not been possible to take advantage of the observed differences in tumour metabolism to produce a very effective chemotherapeutic agent against malignant cells, but one cannot help feeling that it is a reasonable expectation.

In conclusion, it must be confessed that very little has been explained, in any fundamental sense. The reactions which have been explored in this manner are among the simplest of those which go on within the cell, and little can be said as to their remote effects on the more complicated reaches of the synthetic and other metabolic processes of the organism. None the less, a beginning has been made, the direction of further work seems to be indicated, and the prospect which lies ahead staggers the imagination.

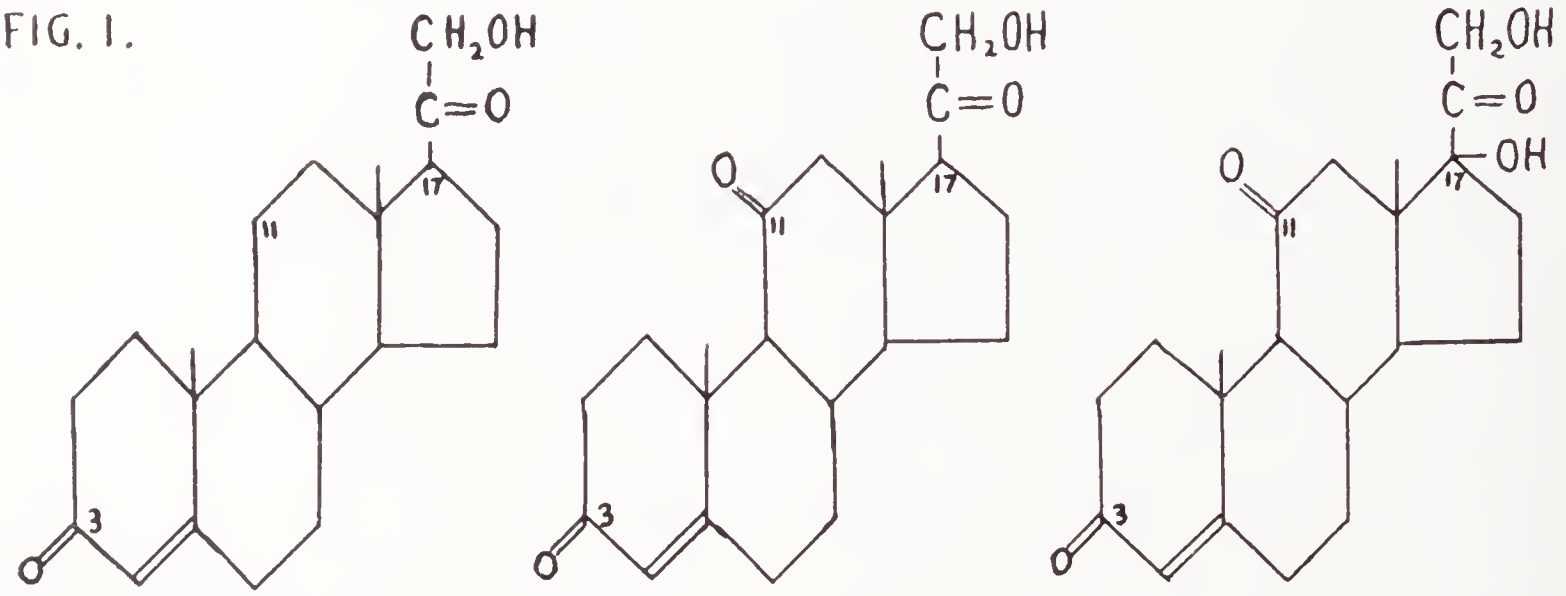
An article dealing with the specific application of some of these principles by Dr. J. G. Watt will appear in a subsequent issue.

THE PITUITARY-ADRENAL RELATIONSHIP

J. S. SPEAKMAN, B.A., 5T2

In view of the current interest in the therapeutic value of certain pituitary and adrenal products, it is worthwhile to re-examine the methods used in studying the interrelationships of these two glands. These methods assess the changes in activity of the pituitary-adrenal system in a variety of experimental and pathological conditions. A thorough knowledge of their physiology is essential to understand intelligently diseases whose aetiology is related to disorders of this endocrine unit.

FIG. 1.



DESOXYCORTICOSTERONE DEHYDROCORTICOSTERONE COMPOUND "E"

EVALUATION OF ADRENAL CORTICAL ACTIVITY

1. Studies of Adrenal Products in Urine

Over twenty sterioids have been isolated from the adrenal gland which are closely related to each other both chemically and physiologically. For purposes of discussion the steroids have been divided into two groups, depending on the presence or absence of oxygen at the C_{11} position. Those possessing an oxygen at C_{11} are primarily concerned with carbohydrate metabolism, those lacking the oxygen with maintenance of electrolyte and water balance. The structures of three important steroids which illustrate this point are shown in figure 1. The maintenance of electlyte balance and the control of carbohydrate metabolism are not separate unrelated functions. It is important to visualize the synergistic action of a number of adrenal factors which demonstrate quite different metabolic effects when administered singly to experimental animals.

The male sex hormone and the adrenal hormones are steroids which, when metabolized, possess a ketone group in the C_{17} position. These C_{17} ketosteroids can be extracted from urine. They react with dinitrobenzene to produce a compound which can be measured colorimetrically. In men the sex hormone may be responsible for 10-20% of the total activity estimated by this procedure. The method, therefore, is not exclusively indicative of adrenal activity.

Pincus has demonstrated a diurnal rhythm in the rate of excretion of 17-

keto-steroids.[9] Greater quantities are found in human urine samples taken during the day than at night. He believes this is due to variations in the degree of non-specific forms of stress. Conditions simulating flying, and flying itself, were found to stimulate keto-steroid excretion. The stress response in psychotic patients was deficient. Fraser has reported high excretion rates in patients with adrenal tumours, and low values of excretion in those with Addison's disease or panhypopituitarism.[3]

Administration of pure steroids concerned with carbohydrate metabolism to adrenalectomized laboratory animals is followed by glycogen deposition in the liver. Dihydrocorticosterone and compound "E" are examples. A method has been devised by Venning and Brown, for extracting from urine active material which has similar properties.[14] The urinary excretion rate was followed in a variety of conditions.[13] Simultaneous ketosteroid analyses were made. Their findings are summarized below.

Clinical Diagnosis	of Keto-steroids	Excretion of Glycogenic Factors
Addison's disease	+	—
Panhypopituitarism	+	—
Anorexia nervosa	+	+
Hirsutism	++++	++
Cushing's syndrome	++	+++++
Pregnancy	++	++++

After surgical stress 3-30 times the normal excretion of glycogenic factors occurred. Typical, and insulin resistant, diabetic patients had similar excretion rates.

In most clinical cases, other distinguishing characteristics are evident and these techniques are not essential for diagnosis. A drawback to the estimation of active material in urine is the fact that only about 10% of intravenously injected material is recoverable. Also, Venning's method does not estimate the secretion rate of salt factors. Thus only an approximation of the true rate of adrenal secretion can be made. Both methods are non-specific since the precursors of the excretory products are not accurately known. In spite of certain defects, these observations indicate that marked changes in adrenal activity can be detected by urine analyses.

Of considerable interest are the mutually independent changes seen in the excretion rate of ketosteroids and the glycogenic factors. Chemical and physiological studies indicate that ACTH (the pituitary factor stimulating adrenal secretion) is a single homogeneous molecule. Thus one might expect the adrenal to respond in a fixed manner, *i.e.*, increases in ketosteroids should parallel increases in the glycogenic factor. This does not seem to be the case, unless there are great variations in the rate of utilization of the different adrenal cortical secretions. This explanation is not satisfactory, and one is forced to conclude that in some instances there is a shift in the type of secretion of the adrenal towards ketosteroid precursors, or glycogenic precursors. It has been suggested that the chemical environment of the adrenal controls the character of its secretory products. No experimental evidence is available to prove or disprove this hypothesis.

2. Studies of Blood Lymphocytes

Single injections of ACTH produce lymphopoenia in rats and mice and an

increase in polymorphonuclear leucocytes.[2] The time relationships of the response are illustrated in Figure 2. This response does not occur in adrenalectomized animals.

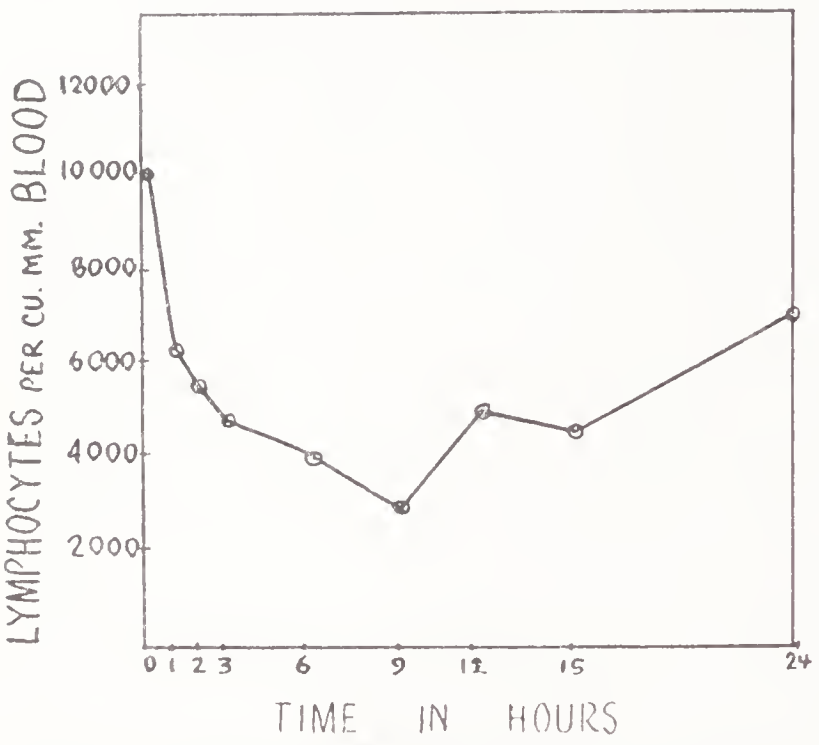


Fig. 2. Lymphocyte changes in the mouse following A.C.T.H. injecton (after Dougherty and White.[2])

Similar changes are produced by injecting cortical extracts. Desoxycorticosterone, however, does not decrease the number of circulating lymphocytes. These experiments indicate that the lymphocyte count can be used as an index of adrenal activity.

Pincus has used these findings to form the basis of an investigation of adrenal cortical secretions in man. He first established that a diurnal rhythm existed in normal men which corresponded to the 17-ketosteroid excretion. A prompt lymphopoenia was observed when high temperatures and humidity, or a pursuit meter, or oral administration of large quantities of sugar, were used as forms of stress. The lymphocytes of psychotic men failed to reflect these stresses. Cortical extracts were injected and caused a typical drop, proving that the lymphocytes were not abnormal. A significant number of psychotic men, however, failed to respond to ACTH, indicating that their adrenal glands were not functioning normally.[8] Studies of psychoneurotic patients on the other hand suggested that the adrenal cortex may become over-labile..

ACTH was thought to be beneficial in many clinical disorders because it stimulated the formation of antibodies from lymphocytes. Recent studies have confirmed the changes in lymphocytes when ACTH is injected but no evidence was obtained to prove that circulating antibody levels were increased.[6]

The study of the changes in blood lymphocytes appears to be a useful means of evaluating adrenal function. One serious disadvantage is its inability to detect the secretion of desoxycorticosterone, a substance of great importance in regulating salt metabolism. The lymphocyte level at any time depends on a balance between the rates of production and destruction of these cells. Several factors other than the adrenal secretion influence this level. Thyrotropic hormone, for example, causes lymphocytosis. One might expect, therefore, to find fairly large variations among individual patients.

3. Studies of Cortical Steroids in Blood

Vogt has estimated the rate of secretion of cortical steroids into the adrenal veins of a variety of experimental animals.[15] Her criterion of activity was the prolongation of survival time of adrenalectomized rats in a cold environment. Aliquots of plasma were injected before the test animals were placed in the cold. Very high values were obtained because of the trauma produced in cannulating the vein. Assays of blood from the right side of the heart and carotid artery

were negative even after evisceration and nephrectomy. This indicates that a rapid destruction of the hormones occurs outside the abdominal viscera. The method is not of practical use, but it is the only technique available for directly estimating the output of the adrenal gland.

EVALUATION OF PITUITARY ACTIVITY

1. Histological Studies

The activity of the adrenal is studied by observing changes in the intact animal or in excreted urine. Factors affecting the secretion of pituitary ACTH are measured by changes in the adrenal gland.

It was an early observation that hypophysectomy is followed by adrenal atrophy. The atrophy is prevented by pituitary injections. The maintenance of adrenal size and structure in the hypophysectomized rat formed the basis for a crude assay of ACTH activity. A great many histological studies to determine the effects of pituitary stimulation on the cellular morphology of the different cortical regions have been made.[4]

2. Chemical Studies of Adrenal Cholesterol and Ascorbic Acid

The adrenal gland has a high concentration of cholesterol and ascorbic acid. Small amounts of injected ACTH produce a rapid fall in the concentration of both these adrenal constituents in the rat and guinea pig.[7]

The time relationships of the response are very similar to those described earlier for the changes in blood lymphocytes. In normal animals a great variety of stimuli have been associated with these chemical changes, *e.g.*, haemorrhage, cold, toxins, pain, scalding and adrenaline injections. The effects of stress, such as haemorrhage, are strikingly similar to the effect of injections of ACTH. They do not occur in hypophysectomized animals. Nothing except exogenous ACTH can depress the adrenal ascorbic acid in these animals. For this reason any change in concentration is taken as direct evidence of pituitary stimulation. This work has made available a rapid specific method for assaying the adrenocorticotrophic hormone.

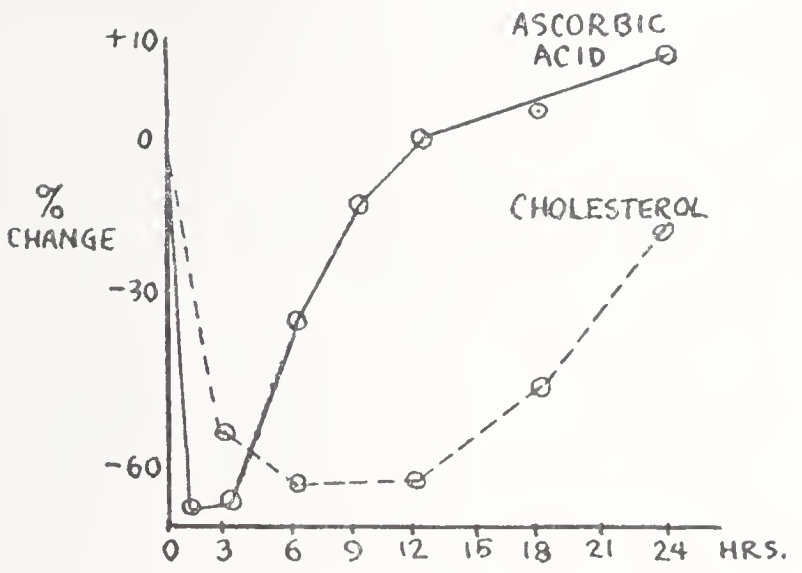


Fig. 3. Adrenal changes in the rat following ACTH injection.

The rate of secretion of the pituitary is inversely proportional to the blood level of adrenal steroids. Injections of cortical hormones prevent the drop in adrenal ascorbic acid ordinarily obtained in normal animals when they are exposed to cold. The inhibiting power of various steroid hormones has been compared. Steroids with and without oxygen in the C^{11} position have this inhibitory property. This influence of adrenal secretions on pituitary function provides a more widely applicable test of steroid activity.

If desoxycorticosterone, a salt factor, is given to rats with demedullated adrenals, it increases their sensitivity to insulin. There is an inhibition of ACTH

release, and hence a release of endogenous adrenal steroids which, through their effect on carbohydrate metabolism, antagonize insulin.[1] Thus, even though there is an acute need for a particular adrenal steroid in the tissues, if others be present in the blood stream the increases in pituitary stimulation which normally occur would be misisng. The normal interrelationship of the two glands has been represented in Fig. 4. (After Sayers and Sayers.[11])

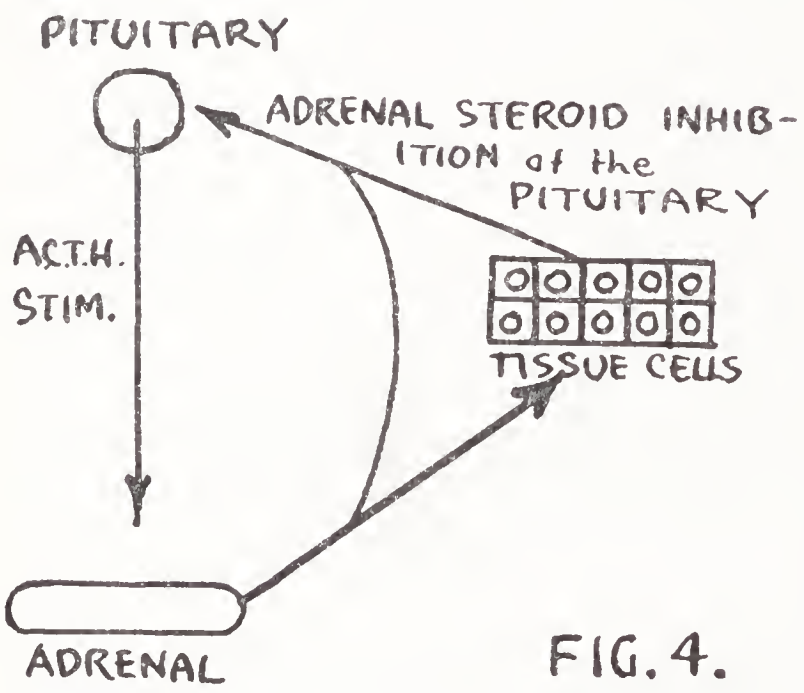
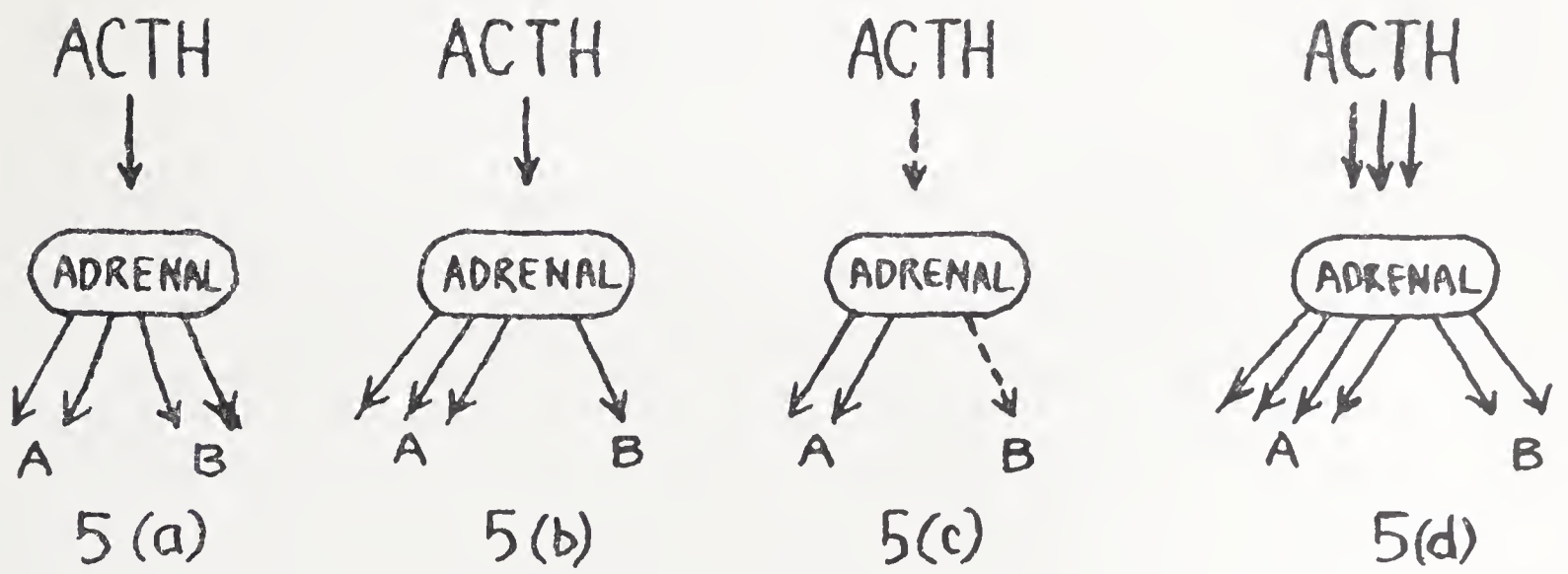


FIG. 4.

When there is an increased utilization of adrenal steroids by the tissue cells there will be a lower concentration in the blood which supplies the pituitary gland. This will result in an increased secretion of ACTH. Conversely, if the rate of utilization is decreased, the resulting pituitary inhibition by the blood steroids will reduce the amount of ACTH released.

These experimental findings can be used to formulate a hypothesis which may help to explain why exogenous ACTH injections are of benefit in certain diseases. Let Fig. 5(a) represent the pituitary-adrenal relationship in a normal individual in whom ACTH stimulation causes a secretion of two factors A and B. If A and B are necessary for the welfare of an individual, then disease may result when either of the two is deficient. Now let us suppose that due to some adrenal abnormality there is a gradual permanent shift in the direction of adrenal secretion towards Factor A. A transitory condition would result in which much more of A and less of B is produced (Fig. 5(b)). Factor A would tend to accumulate through lack of utilization, and inhibit the pituitary secretion of ACTH, thus producing an even greater deficiency of B (Fig. 5c). The individual now exhibits a severe deficiency of essential factor B. If exogenous ACTH is administered the rate of adrenal secretion would be increased considerably. A is produced in excessive quantities and also enough of B to restore the diseased patient to health. Thus, although the original abnormality is not corrected, the deficiencies in the essential factor are remedied by greatly increased adrenal activity. Advantage is taken of the potentiality remaining in the adrenal for producing B. The scheme presented here is an oversimplification. A and B might be groups of substances possessing slightly different physiological activities.

Is there any evidence to support this hypothetical analysis? Pincus has shown that some patients exhibit an abnormal response to stress and ACTH injection. Venning and Browne have found that marked differences in the type of steroid manufactured by the adrenal occur in various physiological and pathological conditions. These findings suggest that changes in the direction of adrenal secretion take place in the body which are not always permanent. Furthermore, Hench has shown that ACTH injections can alleviate the symptoms of rheumatoid arthritis.[5] This must result from altered adrenal function since ACTH



does not produce its characteristic effects in an adrenalectomized animal. Unfortunately, the relief of undesirable symptoms may be associated with elevation in blood pressure, alteration in blood and urine chlorides, electrolyte balance, and excretion of 17-ketosteroids. The side reactions reported are evidence for the overproduction of adrenal steroids (cf. Fig. 5(d)).

Several attempts have been made to isolate ACTH from biological fluids and to determine its potency by the ascorbic acid depletion method. Findings so far have been inconclusive.[12] If the quantity of this material in biological fluids could be measured it would provide a very useful procedure for investigating a variety of endocrine disorders. It might help to clarify the aetiology of those conditions which are treated so successfully with ACTH. Present methods of assessing adrenal function are complicated by the great number of principles elaborated by the gland, some of which are mutually antagonistic. If the simulating pituitary factor could be measured it would simplify investigation considerably. Unfortunately, in urine, pituitary hormones are extremely dilute, and in plasma, are mixed with a great deal of other matter.

The chemical studies concerning adrenal function raise several problems of academic interest. What is the fate of adrenal cholesterol and ascorbic acid? Investigations with labelled cholesterol indicate that it is synthesized into several steroid hormones. The isolation of a steroid-ascorbic acid condensation product from the adrenal has been reported. However, this does not appear to be released into the blood stream since no increase in ascorbic acid activity is found in plasma taken from the adrenal vein.[16] Dugal showed that ascorbic acid administration would prevent the adrenal hypertrophy which occurs when animals are subjected to cold. One of the functions may be the facilitation of adrenal steroid synthesis.

CONCLUSION

The older methods of studying adrenal activity depend almost entirely on qualitative histological procedures, which are extremely limited in their clinical application. Today, however, the quantitative evaluation of adrenal activity by urine and blood analyses makes it possible to estimate the functioning capacity of the adrenal, and to analyze disorders of the pituitary-adrenal system.

Adrenal ascorbic acid changes have been used extensively to measure ACTH liberation in experimental animals. The investigations emphasize the important

role the adrenal gland plays in a great variety of stresses, especially those associated with adrenaline liberation. It has also been shown that the secretion of ACTH is inversely proportional to the concentration of circulating adrenal steroids. Unfortunately, the factors determining the nature of the adrenal response to ACTH stimulation have not been established.

Although a great deal of information has accumulated describing pituitary-adrenal function, it is worth remembering that the mechanism by which the adrenal steroids modify intracellular activity, remains unknown.

REFERENCES

(1) Cheng, C. and Sayers, G., Endocrinology **44**: 400 (1944).
(2) Dougherty, T. F. and White, A., Endocrinology **35**: 1 (1944).
(3) Fraser, R. W. et al., J. Clin. Endocrinology **1**: 234 (1941).
(4) Greep, R. O., and Deane, H. W., Ann. New York Acad. Sc. **50**: 596 (1949).
(5) Hench, P. S. et al., Proc. Staff Meet., Mayo Clin. **24**: 181 (1949).
(6) Herbert, P. H. and De Vries, J. A., Endocrinology **44**: 259 (1949).
(7) Long, C. N. H., Recent Progress in Hormone Research **1**: 99 (1947).
(8) Pincus, G. et al., Psychosomatic Medicine **11**, 74 (1949).
(9) Pincus, G., Recent Progress in Hormone Research **1**: 123 (1947).
(10) Sayers, G., Sayers, M.A., Liang, T. Y., and Long, C. N. H., Endocrinology **38**: 1 (1946).
(11) Sayers, G. and Sayers, M.A., Ann. New York Acad. Sc. **50**: 509 (1949).
(12) Taylor, A. B., Albert, A. and Randall, G. S., Endocrinology **45**: 335 (1949).
(13) Venning, E. H. and Browne, J. S. L., Ann. New York Acad. Sc. **50**: 627 (1949).
(14) Venning, E. H., Hoffman, M. M. and Browne, J. S. L., Endocrinology **35**: 49 (1944).
(15) Vogt, M., J. Physiology **102**: 341 (1943).
(16) Vogt, M., J. Physiology **107**: 239 (1948).

DIABETES INSIPIDUS[1]

RAOUL KOURILSKY[2]

HUMAN DIABETES INSIPIDUS is generally regarded as being a condition characterized by primary polyuria and secondary polydipsia, which can be caused by various lesions in the hypothalamo-pituitary region and which can be markedly alleviated by the administration of posterior pituitary extract. Early physiological research established the role of neural and endocrine factors in the aetiology of the polyuria. It could be produced by experimental lesions in the floor of the fourth ventricle, the hypothalmus, or the posterior lobe of the pituitary gland which secretes an antidiuretic hormone acting directly on the renal tubules. The supraoptic nucleus, the hypothalamic tract and the posterior lobe of the pituitary gland have been proven to function as a neurophysiological unit (1). The importance of these findings to an understanding of the polyuria of diabetes insipidus is emphasized by the diversity of hypothalamo-pituitary lesions due to trauma, surgery, tumours, or inflammation, which can result in clinical cases of the disease. Generally, the thirst has been attributed to the dehydration resulting from the polyuria, an explanation also supported by physiological research, and thus an apparently coherent and logical concept of diabetes insipidus was formed which has been almost unanimously accepted: a hypothalamo-pituitary lesion causes a decreased secretion of the antidiuretic hormone with consequent polyuria and the resultant dehydration causes the thirst. Recent clinical experience, however, has shown that this concept does not explain all cases satisfactorily and has lead to the following conclusions: (*a*) polydipsia is not necessarily the result of polyuria, and the two can be dissociated; (*b*) cases of diabetes insipidus in which polydipsia predominates are far more numerous than those in which polyuria predominates; and (*c*) the two forms can be differentiated clinically and biochemically.

Usually, in man, it is not possible to determine which of the symptoms appeared first; however, in some cases in hospital for other conditions, a marked thirst was noted some hours before the onset of polyuria and the development of diabetes insipidus (3). In addition, a patient with post-traumatic diabetes insipidus described an immediate amelioration of thirst during the tapping of a sub-arachnoid cyst at the base of the brain which had elevated the hypothalamus and stretched the pituitary stalk. This was followed by a return of the urinary output to normal. Thus, in some cases, polydipsia has been demonstrated to occur first without at least clinically demonstrable antecedant polyuria. Polyuria then sets in apparently only as the expected increase in urinary excretion following the increased water intake. This dissociation of the two symptoms can be even more marked so that the polyuria is always less than the polydipsia, the excess fluid being eliminated by the skin. Such observations indicated that a certain number of cases of diabetes insipidus exists in which thirst is the predominant symptom and polyuria appears to be merely

[1]Condensed from a paper of the same title originally presented in a series of lectures to the Fourth Medical Year, Spring 1949.

[2]Professeur Agrégé à la Faculté de Médecine, Médecin des Hôpitaux, Paris, France.

the consequence of the increased water intake.

A water-intake restriction test was employed to ascertain the exact proportion of such cases. During it, the patient was put on a well balanced, low-salt diet providing 2100 Calories, 789 Grams of water and only 2.5 Grams of salt, and the patient's weight and the volume of urine excreted were measured at regular intervals over a period of several days during which the patient was kept under continual observation. The test was stopped if, after 24 hours, the water loss was too great or if it was regular and continuous. At the end of the test-period, the patient was then permitted to drink as much water as desired and also given an injection of ten units of posterior pituitary extract. During this test it is important to avoid excessive dehydration of the patient and it must be remembered that rehydration can be accomplished only by water given orally. The intravenous injection of saline or glucose solutions only aggravates the state of dehydration.

In seventy-eight percent of forty patients, it was found that such a restriction of liquids was followed by an essentially parallel decrease in urine excretion, and thus, that there was no apparent pathological renal cause for the polyuria. In most of the others, a ninety percent reduction in the water-intake was accompanied by a decrease in urine excretion of only from thirty to fifty percent, and diuresis continued at the expense of a loss of tissue fluids. These results (4) confirmed the existence of two types of diabetes insipidus: polydipsic and polyuric.

A well-conducted restriction test enables the clinician to classify cases of diabetes insipidus into these polyuric and polydipsic types, to subclassify the latter into pure and mixed forms, and to ascertain, therefore, the approximate extent of the secretory deficiency of the posterior lobe of the pituitary—complete in the polyuric type, partial in the mixed polydipsic form, and not in the rarer cases of pure polydipsia.

When studying the biochemical changes which occur in diabetes insipidus, it is important to remember that whatever may be the type, any patient suffering from the disease inevitably shows some disturbances brought about simply by the excessive intake of water quite apart from any others due to the disease itself. Even the changes in the urine and blood findings in normal subjects following prolonged, massive intake of water vary widely and depend particularly upon individual differences in the regulation of water balance. No reliable classification of diabetes insipidus can be established on the basis of any one chemical change, for example, the plasma protein concentration or the urinary chloride excretion, as has been attempted by some authors.

In the polydipsic forms, where restriction of fluids is accompanied by a parallel reduction in the urinary excretion, there are no constant biochemical changes characteristic of the condition and those which do occur ressemble those observed during increased fluid intake in the normal person. Thus, there are no special criteria for the diagnosis of the polydipsic forms of diabetes insipidus other than the changes observed during the restriction test.

In the polyuric type, characteristic chemical changes, such as an increase in the plasma protein concentration, do occur. In practice, however, the diagnosis of the polyuric type of diabetes insipidus can be most readily established on the basis of three findings: (*a*) during

the restriction of water, the specific gravity of the urine, though increasing from 1.001-1.002 to 1.008-1.010, is still low; (*b*) posterior pituitary extract is rapidly effective and remarkably potent; and (*c*) salt aggravates the condition and a high-salt diet during the restriction of fluids is poorly tolerated and can be dangerous.

In neither type is the intensity of the thirst, the volume of water taken, or the excess of water excreted as compared to that taken of any diagnostic significance.

Cases of the true, polyuric type of diabetes insipidus are the most rare (sixteen percent of thirty cases). The condition occurs as a result of a complete loss of secretory function in the posterior lobe of the pituitary gland with the preservation of function in the anterior lobe. The polyuria is but slightly reduced during the water restriction test. In the blood, there is an hyperchloremia and hyperproteinemia and other evidence of dehydration. Posterior pituitary extract immediately and completely alleviates the condition.

In the polydipsic type, two forms may be distinguished, as noted above: (*a*) pure polydipsia, (twenty percent of thirty cases), in which no particular clinical findings, not even a favorable response to the administration of posterior pituitary extract, can be observed to enable distinguishing the condition from a voluntary increase of water-intake in a normal, healthy individual, and (*b*) mixed polydipsia (sixty-four percent of thirty cases), in which posterior pituitary extract has a more or less favorable effect, the excretion of salt is variable, and the urinary specific gravity during the restriction test is not particularly high (1.011-1.020).

Detailed histological studies (6) have established that, in man, partial destruction of the hypothalamo-pituitary tract or partial supression of posterior pituitary function due to any cause is associated with polydipsia without clinically evident polyuria. Thus the lesion giving rise to polydipsia is of no constant type. Instead, mixed polydipsia represents the most frequent expression in man, of any partial depression in the functioning of the supraoptic-posterior pituitary mechanism.

Apparently, polydipsia can occur in the absence of any lesion in the hypothalamo-pituitary region. This re-opens the question of "psychogenic polydipsia." In most cases, however, it was possible to demonstrate some extrahypophyseal disease such as an intracranial infection, for example, encephalitis or meningitis, or a lesion of a frontal lobe. It must be emphasized, however, that the psyche of the patient suffering from an hypothalamic lesion readily influences the intensity of the thirst and that, probably, disturbances in the function of the cortico-hypothalamic tracts may also affect the psychic state of the patient.

True polyuria is observed only when the function of the hypothalamic-posterior pituitary unit is completely suppressed, while that of the anterior lobe of the pituitary is preserved (2), as when there is bilateral destruction of the two supra-optic hypothalamic tracts, or practically complete destruction of the posterior lobe of the pituitary gland. Both of these conditions are found only rarely clinically. The partial lesions are the most frequent and as long as the destruction is incomplete, marked diuresis does not occur.

Posterior pituitary extract can be effective only when there is a definite decrease in posterior pituitary function.

The extent of its effect parallels this decrease and, therefore, a partial but definite improvement in polydipsia may result in cases with partial lesions upon the administration of posterior pituitary extract. Likewise, the degree of change in the urine specific gravity during the restriction test and the untoward effects of salt in the diet vary in proportion to the degree of disturbance of posterior pituitary function even in the absence of polyuria.

It is interesting to note that in man, the first clinical symptom of any partial decrease in the activity of the hypothalamo-posterior pituitary unit is polydipsia and not polyuria whereas all experimental studies have laid stress on the polyuria. This does not mean that renal tubular function is normal. It is not; but clinically, the disturbance in tubular reabsorption in itself is insufficient to induce polyuria whereas the partial reduction in posterior pituitary function is sufficient to induce thirst. In consequence, the organism is "flooded" by the increased amount of water taken and the resultant polyuria becomes as conspicuous a symptom as the polydipsia.

Thus, the regulation of thirst in man is more readily disturbed, clinically, by pathological disorders of the hypothalamo-pituitary region than is the regulation of renal tubular function. The exact mechanism for the control of thirst remains uncertain despite considerable research and the elaboration of several theories regarding it. Clinical studies on the cases which have provided the basis of this paper have shown that: (*a*) thirst need not be the direct consequence of dehydration; (*b*) in man, the part played by local sensation in the mouth and its relation to salivary secretion appears to be an important factor in determining the degree of thirst; (*c*) salt is also an important factor; and (*d*) the effect of the posterior pituitary gland on thirst is secondary to its effect on renal excretion.

In the regulation of renal tubular function, only minute amounts of the posterior pituitary antidiuretic hormone are necessary profoundly to influence tubular reabsorption and, therefore, to regulate the degree of diuresis. The regulation of secretion of the hormone, in turn, is related to the function of very sensitive osmoreceptors (7).

During the treatment of diabetes insipidus, in addition to the administration of appropriate amounts of posterior pituitary extract, a salt-free diet should always be prescribed. It decreases the amount of the extract necessary to ensure hormonal balance, and it decreases the intensity of the thirst.

Infections of the nasopharynx, particularly the nasal sinuses, were found to be responsible for the majority of cases of diabetes insipidus in which the usual causes (trauma, tumour, neurosyphilis, or encephalitis) could not be found (5).

W.G.B.C

REFERENCES

(1) Fisher, Ingram, and Ranson: *Diabetes Insipidus*, Edward Bros., Ann Arbor, 1938; Arch. Neurol. Psychiatry **34**, 124 (1935).
(2) Heimbecker and White: Ann. Surg. **110**, 1037 (1939); Amer. J. Physiol. **133**, 582 (1941).
(3) Kourilsky: Bull. Mém. Soc. Méd. Hôp., Paris, **65**, 718 (1941); Ibid. **66**, 115 (1942); Rev. Neurologique **74**, 261 (1942).
(4) Kourilsky, Corre, Mignot: Bull. Mém. Soc. Méd. Hôp., Paris, **68**, 435 (1944); Ibid. **69**, 15, 20 (194).
(5) Kourilsky and Kourilsky: Ibid. Séance du 28 Juin, 1946, p. 380.
(6) Roussy, Kourilsky, and Mosinger: Rev. Neurologique **78**, 313 (1946).
(7) Verney: Lancet, 1946, **ii**, 739, 781.

A PROBLEM IN DIAGNOSIS, PART I

T. A. McLENNAN, 5T0

PRESENTATION OF CASE

G.R., A FIFTEEN YEAR OLD, white schoolgirl, was admitted to the Medical Service of the Toronto General Hospital on September 24, 1949. A tentative diagnosis of patent ductus arteriosus with subacute bacterial endocarditis had been made by the family physician.

Excellent health had been experienced by the patient until June 1949 when she first noticed episodes of sharp chest pain brought on by laughing, and felt at the anterior end of the second left interspace. By early August, spontaneous, more severe, deep aching pain was noted, especially in bed at night. Radiation to the left shoulder and down the arm to the left elbow sometimes occurred. The pain, lasting several hours and relieved by a hot water bottle, would recur every two or three days. In mid-August her doctor ordered a miniature chest film which was reported to him as showing cardiac enlargement. At this time mild sweats, chills, increasing weakness and malaise, occasional orthopnoea, persistant low-grade fever, slight leucocytosis and the presence of a cardiac murmur suggested the above-mentioned diagnosis. Blood cultures were negative. The patient was given a triple-sulpha preparation and then six million units of penicillin intramuscularly during a five week period, but the course of her illness was not affected. Early in September she had five severe nose-bleeds. A mild, irritating cough, productive of half a cup of white sputum daily, was first noted in mid September, a week prior to admission.

Examination on admission revealed a pale, rather thin girl, who had lost no weight during the four months of her illness. She looked chronically ill and coughed frequently. The oral temperature was 100°F, pulse rate was 110 per minute, blood pressure was 120/80, weight was 98 pounds, respiratory rate was 18 per minute.

Significant physical findings were limited to the left chest. The trachea was not shifted. A fullness could be seen below the left clavicle. Left chest expansion was limited. The patient's deep aching pain could be reproduced by pressure over the sternal end of the second left interspace. Decreased tactile fremitus was present over the left upper chest anteriorly and the left lower chest posteriorly. Over the lower two-thirds of the left lung percussion was dull and the breath sounds were diminished. Above this level breath sounds were harsh. Medium râles could be heard at the left apex, left axilla and the left base posteriorly. There was no sign of visible, superficial thoracic veins, jugular distension, cyanosis or clubbing of the fingers. The right border of the heart and its point of maximum impulse were normally placed. The heart sounds were regular in rhythm and of normal intensity. A moderately loud pulmonary systolic murmur could be heard best with the patient lying flat, but no thrill was palpable.

Laboratory examination revealed a normal urinalysis, a haemoglobin of 68%, a white blood count of 13,800 with 83% polymorphonuclears and no abnormal cell forms in the smear, a Westergren sedimentation rate of 94 mm. in one hour. The blood Wassermann, Aschheim-Zondek test, tuberculin test, Brucella

and enteric organism agglutinations, and blood cultures were negative.

X-rays taken in hospital could be compared to a normal miniature film taken during a routine survey of school children in March 1949 and to the miniature film taken on August 18, 1949 which erroneously was thought to show cardiac enlargement. The hospital films revealed a large, lobulated, fairly translucent mass, with smooth edges; it extended from the mediastinum into the left half of the chest at the mid-sternal level. Antero-posterior laminagrams localized it to the anterior mediastinum. No bone erosion was seen.

An aspiration biopsy revealed striated muscle fibres. A second biopsy showed the presence of necrotic tissue which, it was felt, might have originated in the lung.

SUMMARY

A fifteen year old girl presents with localized left-sided chest pain, that has increased in intensity for four months. Low grade fever, sweating, chills, slight orthopnoea and cough appeared in the six weeks before admission. On examination there is a fullness below the left clavicle and left chest movement is limited. Dullness to percussion is present over the lower two-thirds of the left lung and breath sounds are diminished in the same area. Medium râles are heard at the left apex, the left axilla and the left base posteriorly. There is a moderately loud systolic murmur in the pulmonary area. Radiologically a mass is seen in the anterior mediastinum, at the mid-sternal level, extending into the left lung field.

(*Continued on Page 155*)

CANADIAN CANCER SOCIETY FELLOWSHIPS

The Canadian Cancer Society announced on November 30, 1949, establishment of medical fellowships in memory of the late Doctor Allan Blair of Regina. The fellowships are for study of the diagnosis and treatment of cancer.

Each of the two fellowships has a value of $4,000 per year for two years. The first becomes available July 1, 1950, the second July, 1951, and in rotation thereafter.

Applicants, in addition to a medical degree, must have not less than three years of postgraduate study, of which at least two shall have been in a field related to the diagnosis or treatment of cancer.

According to the conditions which have been established, fellows shall express a firm interest and assume the moral obligation to practice his or her profession subsequently in Canada with a particular interest in cancer.

THE DUTIES OF A SUMMER CAMP PHYSICIAN

MARTIN G. WOLFISH, M.D. 4T9

THE PAUCITY OF LITERATURE dealing with the duties of a summer camp physician and the maintenance of a summer camp infirmary is quite apparent. Summer camp medical care is in the hands of senior medical students and young doctors in the large majority of instances, and it is to them that I would address my remarks. This type of work is most interesting, instructive, and gratifying.

The author was engaged as a camp physician at a summer camp* operated by a community organization. The capacity of the camp was 130-150 children in three periods of three weeks each—a total of 345 children. There were also approximately 35 staff members, including counsellors and administrative, kitchen and maintenance staffs.

The duties of a camp physician are, basically, the maintenance of an optimal level of health in this community of children and adults, and the diagnosis and treatment of accidents and illnesses as they occur. By far, the former is the more important—many of the illnesses seen at a summer camp are preventable, and the incidence of morbidity may be kept to a minimum if potential causative factors of disease are found and, if possible, are eliminated. In a more detailed breakdown, these duties usually consist of the following: (*a*) examination of campers on arrival at camp and on departure, (*b*) medical attention at sick-parade, in emergencies and for hospitalized patients, and (*c*) the general supervision of camp hygiene.

EXAMINATION OF CAMPERS

The camp at which I was employed required that each child be examined by his family physician within 48 hours of departure for camp. A standard form was to be filled out detailing past illnesses, immunization records, A.T.S. administration, physical examination, and any instructions that the physician may want to give the camp doctor. After examination of over 300 of the pre-camp medical forms I came to the disheartening conclusion that many were useless; the doctors had completed these forms either without seeing the child at all, after a telephone conversation with the parent, or after only a very cursory examination. The value of this pre-camp examination cannot be underestimated. Properly performed, it would lessen the incidence of children arriving in camp with contagious diseases, and would also furnish the camp physician with a concise, but valuable, past health record of the individual.

Within a day or two of arrival each child was seen by the camp physician and underwent the usual periodic health examination. The child was weighed and the height was taken. An examination was made of the skin, hair, eyes, ears, nose, throat, respiratory system, cardiovascular system and the feet. The value of a rather complete examination on arrival at camp is evident. Should the child become ill while at camp, an accurate record of his state of health on arrival is available. Any defects found on this examination that were not already known by the child's parents can be reported to them. Since this group of children was fairly representative of the general population of that age, both economically and socially, an

*Camp B'nai B'rith, operated by the Jewish Camp Council of Toronto.

analysis of the results of this examination is presented in tables I, II and III.

The high incidence of children previously immunized against smallpox, diphtheria and whooping cough is a measure of the success of preventive paediatric practice exercised in early childhood. The few children not previously immunized were mainly from Europe, and were recent arrivals in this country.

TABLE I

DISTRIBUTION OF CHILDREN* ACCORDING TO AGE

Age in Years	Number
6½	1
7	8
8	53
9	45
10	66
11	44
12	62
13	44
14	17
15	5
	–
Total	345

*All female.

EXAMINATION BEFORE LEAVING CAMP

The day before the children left for home, each child was re-weighed. In this way we were able to determine weight losses and gains throughout the stay at camp. Significant gains and losses were those over three pounds (with the child wearing the same clothing as when she was previously weighed).

Significant gains were found mainly in those children who were undernourished on arrival at camp, but weight losses, when they occurred, were consistent throughout cabin groups, usually older girls who fancied that they must diet. There was little relationship between weight losses and children who were found to be obese on arrival. At this examination, children who had recently been at sick-parade were again checked and if medical attention had to be continued at home, a letter was sent to child's parents.

TABLE II

PHYSICAL DEFECTS FOUND ON EXAMINATION

Defect	Number of Cases	Percentage of Campers
Epidermophytosis of feet	30	8.9
Excess wax in ears	29	8.9
Undernourishment	25	7.1
Obesity	23	6.9
Chronic tonsillitis	22	6.9
Dental Caries*	22	6.9
Refractive errors†	9	2.6
Otitis externa	4	
Allergic rhinitis and hay fever	4	
Scoliosis, idiopathic	3	
Scabies	2	
Mental retardation	2	
Post-mastoiditis deafness	2	
Stuttering	1	
Habit spasm	1	
Hallux valgus	1	
Colloid goitre	1	
Funnel chest	1	
Rheumatic heart disease	1	
Functional systolic murmur	1	
Exophoria	1	
Harelip and cleft palate‡	1	
Coxa vara	1	
Adolescent Kyphosis	1	
Total	188	

*Dental defects include those that were visible on inspection of the teeth. No detailed probing was attempted.

†The only refractive errors noted were those that had previously been diagnosed and corrected with glasses before arrival at camp.

‡Successfully treated surgically at the age of 18 months.

TABLE III

IMMUNIZATION HISTORY

Disease	Number of Children	Percentage of Campers
Smallpox	343	99.9
Diphtheria	341	99.9
Whooping cough	318	92.2
Scarlet fever	34	10.0
Tetanus	32	9.2
Typhoid fever	4	1.2

MEDICAL ATTENTION

Sick parades were held twice daily for children who felt ill or who were on treatment. The infirmary was open at all times for emergency cases. The medical staff saw all the accidents and illnesses that occurred in camp except minor incidents, such as mosquito bites, mild sunburn, scratches and small cuts. These were handled by the individual counsellors with the aid of a First-Aid Kit. All visits to the infirmary were recorded doubly. A "Daily Health Report" was kept, listing the names, complaint, diagnosis and treatment of all cases seen. In addition, the visits were also recorded on the individual camper's health records. In this way the health of the camp could be studied from day to day as a group, and longitudinally for each individual.

Table IV lists, in order of frequency, illnesses and accidents seen during the summer.

Upper Respiratory Infections included acute pharyngitis, nasopharyngitis, tonsillitis, and laryngitis. It was quite evident that once a case occurred within a cabin it spread rapidly throughout the entire cabin group. This was probably due to the close proximity of the beds. I could find little relationship between inclement weather and the incidence of colds.

TABLE IV

ILLNESSES AND ACCIDENTS SEEN DURING THE SUMMER

	Number of Cases	Number of Visits
Upper respiratory infections	210	582
Minor accidents	138	170
Gastro-intestinal complaints	64	67
Headache	45	52
Styes	20	32
Conjunctivitis	11	28
Other eye complaints	13	28
Boils and infected wounds	32	79
Earache	24	43
Psychological complaints	20	20
Sprains, etc.	18	24
Epidermophytosis	12	15
Miscellaneous	133	213
Totals	770	1353

Minor accidents included splinters, bruises, cuts, scratches and abrasions. A fair percentage of the cases that actually occurred were treated by the counsellors and were not seen at the infirmary.

Gastro-intestinal complaints included gastritis, colic, suspected appendicitis, constipation and gastro-enteritis. The majority of cases of gastro-enteritis were functional in origin and were found in older campers and in counsellors showing other signs of emotional instability.

Earaches were mainly due to secretory otitis media due to Eustachian salpingitis, a frequent accompaniment of upper respiratory infections. Other cases were due to otitis externa, impacted cerumen or furunculosis. No cases of suppurative acute otitis media were seen.

Under the heading of sprains are included sprained ankles, sprained wrists, two cases of torn internal lateral ligament of the knee, and several severe bruises to the coccyx. Most of the more severe sprains were taken to the town hospital for X-ray to rule out fracture. Fortunately, no fractures occurred during the camp season.

The number of cases of epidermophytosis seen at sick-parade represent only a small percentage of the cases that actually occurred. These were found at the initial examination and were treated at the cabin by the child herself or her counsellors. Fungicidal ointment and powder (Desenex) were supplied to each case and instructions given as to their use.

HOSPITALIZED CASES

Children who required bed rest and nursing care were confined to the infirmary hospital ward. This ward was equipped with five beds and adequate facilities for nursing care. Hospital charts were kept for each patient listing temperature, pulse, respiration, medication, etc. The commonest cause for hospitalization was upper respiratory infections, as shown in table V.

A word should be said about dehydration. These children were admitted complaining of headache, general malaise, and fatigue. The only findings were tachycardia, fevers (ranging from 101-104°F.) and the signs of dehydration, such as dry tongue and skin. With no specific therapy, but with rest and forced fluids, these symptoms disappeared and the temperatures fell to normal within 2-3 hours. There were no relapses once the fluid requirements were met and subsequently maintained. On enquiry this seems to be a fairly common reaction in summer camps where drinking facilities are not always close at hand, the children are actively engaged in exercise and a large area of skin surface is exposed due to the scanty attire usually worn.

TABLE V

CAUSES OF HOSPITALIZATION

	Number of Cases	Average Number of Days in Hospital
Acute pharyngitis	10	1.4
Acute nasopharyngitis	6	2.0
Acute tonsillitis	3	1.6
Acute sinusitis	2	1.0
Dehydration	4	1.0
Scabies	2	2.0
Fatigue reactions	2	1.0
Submandibular lymphadentis	1	6.0
Acute cystitis	1	15.0
Fever (undiagnosed origin)	1	4.0
Heat prostration	1	1.0
Functional gastroenteritis	1	0.5
Suspected appendicitis	1	0.5
Abdominal colic	1	1.5
Total	46	

SUPERVISION OF GENERAL CAMP HYGIENE

This included the supervision of food preparation, food storage, dish-washing, garbage disposal, latrine and washroom sanitation, water and milk supplies, and general camp cleanliness. The kitchen and refrigerator were inspected daily. The condition of food, floors, walls, stove and utensils were checked. With the co-operation of the kitchen staff in keeping the kitchen and refrigerator clean no illness of any sort could be traced back to the kitchen.

The camp had a fully screened garbage shed and this did much to prevent any garbage disposal problem. No flies were seen around garbage at any time. The garbage was removed daily from the shed to the incinerator by the camp handyman.

The condition of the latrines and washrooms were also checked daily. It is the responsibility of a camp physician to see that the maintenance staff keep the toilet facilities in a clean condition and the plumbing in working order.

Supervision of water and milk supply is a most important function of a camp physician. The majority of summer camps draw their water supply from a well, spring or lake, and chlorinate it before use. The most practical method of chlorination is by the use of a hypochlorinator pump using solutions of sodium hypochlorite or chloride of lime as the source of chlorine. In smaller camps, the water supply can be chlorinated manually with these same reagents. The chlorine content of the drinking water can be easily checked daily with an orthotolidine colorimeter—a simple and inexpensive method. Bacteriological checks on the water should be done at the beginning of the summer and at two or three week intervals depending on the quality of the supply. Samples of both raw and treated water should be submitted to the Public Health Laboratories for examination.

Since pasteurized milk is universally purchased in Ontario, no problem should arise other than that of storage. If milk is purchased in quart bottles, the problem of left-over milk is negligible, but if, for reasons of economy, milk is purchased in larger cans and is served in pitchers, unused and left-over milk must be carefully guarded to prevent contamination and souring. It is unnecessary to stress the importance of proper refrigeration and prevention of contamination of milk.

OTHER ACTIVITIES

The camp physician is looked upon as an integral part of the camp and enters into camp programming and activities as the opportunity presents itself and as time permits. By virtue of his medical training and interest in things of a scientific nature, the doctor may enter into such activities as first-aid talks, nature study groups, sex discussions, etc. Reciprocally, these are of value to the camp physician. Children meeting the doctor under circumstances not related to medical care will be far less apprehensive when and if the occasion arises that they must see the doctor when ill.

By perusal of the figures included in this paper it will be evident that the camp physician will not meet many of the usual and more serious cases seen in the hospital as a student or interne, but will meet many illnesses of a less serious nature. It is for these that the family doctor is most often called upon to treat, and for which the medical student has but little opportunity to study during his undergraduate years.

SCLERODERMA

LOIS A. LLOYD, M.D., 4T9

THE DISEASE SCLERODERMA is also known as hide-bound disease, or dermatosclerosis. It has been divided into acute, subacute, and chronic forms, and further subdivided into duffuse, symmetrical, and circumscribed types. The latter, when it involves the extremities, is known as acrosclerosis. A further modification, known as "white spot disease," is characterized by elevated "pin-to-pea" sized dead white plaques.

AETIOLOGY

The aetiology of the disease is unknown. Wurthele-Caspe has described an acid fast organism, "sclero acillus," in nasal scrapings, and blood cultures isolated 5 out of 6 cases. The possibility of a common aetiology, either bacterial or resulting from a hypersensitive state, has been discussed with regard to scleroderma, disseminated lupus erythematosus, Libman Sach's syndrome, periarteritis nodosa, rheumatic fever, rheumatoid arthritis, thromboangiitis obliterans, and serum sickness. Such diffuse collagen diseases may show collagen degeneration in the walls and lumina of blood vessels; in endocardium, pericardium, pleura, articular and periarticular tissue, and, in fact, any connective tissue in the body—thereby resulting in many manifestations of the lesion. Allergy has been suggested as the cause in all these conditions, because experimental hypersensitivity has produced similar fibrinoid degeneration.

PATHOLOGY

The keratin and squamous cell layers of the skin appear normal. The basal cell layer may be flat or heaped up. In the superficial cutis there is slight perivascular infiltration and fibroblasts, lymphocytes, plasma cells and bands of fibrous tissue are present. In the deep cutis there is marked perivascular infiltration. Thickened collagen forms fibrous bands; in some areas fibrinoid degeneration is seen. Clear areas are seen between collagen and interstitial areas (when stained with haematoxylin and eosin). Fenestrations about the blood vessels and hair follicles stain red with special cresyl violet stain.

In the kidney there may be a wire loop appearance in the glomeruli and occasionally necrosis and swelling of the basement membranes occur.

Vegetations free of bacteria and Aschoff bodies may occur in the heart valves.

The first change is in connective tissue, later in elastic tissue and finally in blood vessels.

CLINICAL PICTURE

Clinically, diffuse scleroderma is commoner in females (2: 1) and in childhood, early adult life and, occasionally, in neonatal life. Characteristically, cutaneous manifestations begin in the periphery—hands, feet, bridge of nose and cheeks; they extend slowly to involve all parts of hands, face and trunk. At first the fingers stiffen and the mouth puckers. The skin becomes smooth and tight and adheres to the deeper structures.

There may or may not be previous attacks of vascular spasm in the hands, as occurs in Raynaud's disease. Occasionally, there is a low grade fever without intercurrent infection; usually the temperature is normal.

Sclerosis of the skin leads to complete immobility of the joints of the fingers, hand, maxilla, and larger joints.

The phalanges show rarefaction due to interference with circulation of the digital arteries, and the peripheral ends may atrophy to mere points. Fibrosed and degenerated periarticular tissue of the phalanges may be heavily infiltrated with lime, and form large periarthritic tophi.

Areas of brown pigmentation may appear on the dorsum of the extremities.

In the skin, diffuse sclerosis occurs in the epidermis and the subcutaneous connective tissue. Similar sclerotic changes may occur in the connective tissue of the oesophagus and interfere with its mobility.

Dr. Vallee described the typical picture of scleroderma as starting with a febrile illness, e.g., influenza, sore throat, tonsillitis, or scarlet fever, followed by a free period lasting days or months when the patient feels perfectly well. Then oedema of the extremities, malaise, myalgia, or a low grade fever occur. The face, neck, thorax, legs and buttocks show pallor and swelling. The mobility of the face is lost, and the dull waxy swelling, and masklike appearance resemble Parkinsonism. The eyelids may be swollen and red, and the conjunctivae thick and elevated, the oedema ending abruptly at the cornea.

The oedema is pale, hard, and nonpitting, the skin is thick and indurated. An erythematous rash on the arms and face may occur, and the normal skin markings may be exaggerated. The dermal appendages remain normal.

Rarely the tongue and pharyngeal tissue are involved causing dysarthria and dysphagia. Stiffening of the skin of the thorax may lead to dyspnoea. Hydrothorax, hydrarthrosis, and occasionally pleural and pericardial effusion occur. The nails may show an increase in the lunar area and thinning of the cuticle.

COURSE OF THE DISEASE

Progressive restriction of mobility usually occurs. The maximal area of skin involved is reached early, then gradual regression occurs in one to six months. The duration of oedema is unpredictable. Islands may resolve in years, and relapses are known to occur after thirteen to twenty years. Ulceration of the finger tips, contractures, deglutition, and generalized profuse fibrosis of internal organs and skin offer a grave prognosis. Complete recovery or persisting atrophy may result. After years of progressive debility, or exacerbations and remissions, death results.

LABORATORY FINDINGS

The Wassermann reaction may be positive without history or evidence of syphilis; the BMR may be high, normal or low; the urine is normal; total protein, albumin, globulin, chlorides, sugar, calcium, phosphorus in the blood and glucose tolerance test are normal.

DIFFERENTIAL DIAGNOSIS

This includes *dermatomyositis*, characterized by muscle pain, weakness and atrophy, fever, erythematous, skin lesions, increased sedimentation rate and progressive crippling and incapacity; *myxoedema*, characterized by low BMR, low blood cholesterol, and quick response to dried thryoid; *trichinosis*, characterized by muscle tenderness, eosinophilia, fever, localized oedema, and positive skin and complement fixation tests; *oedema* of cardiac, renal or hepatic disease. Other diseases to be ruled out include *Raynaud's disease*, *carcinoma "en cuirass,"*

leprosy (which shows no induration), *amyloidosis*, and *calcinosis*.

TREATMENT

The multiplicity of suggested treatments signifies the inadequacy of any one method. Various authors have reported good results with *Vitamin D*. The suggested dose is 3 cc. of Dihydrotachysterol (vit. D) orally for 12 days. This treatment has been successful where parathyroid deficiency is the cause. 500 mgm. of *Benadryl* daily for 6 months has helped to soften skin and heal ulcers in certain cases of acrosclerosis. 5% *Bromine* in Tragacanth, intravenously, was advocated by Dr. Wuerthele-Caspe. *Anterior Pituitary Extract*, 1 cc. every second day, has given good results in some cases; Posterior Pituitary Extract has been used. Dessicated *Thyroid* may be helpful in extensive cases. *Sympathectomy*, to relieve vasospasm, probably has been successful in many cases.

Other methods of treatment include tonics composed or Iron, Arsenic, Cod Liver Oil and Ammonium Chloride to remove excess calcium; Pilocarpine, in dry cases; Sodium Salicylates, Gold and Bismuth intramuscularly, Ovarian Extract, mildly stimulating ointments (such as Oil of Turpentine, 20%, in Lanolin, and Mercury, Soap or Chloroform Ointments) and ortho-haemotherapy have been tried. Massage and passive movements plus advice to avoid extremes of temperature have been given.

For ulcers, Acid Fuchsin (5 parts) in Oil of Eucalyptus (25 parts) and Lanolin (100 parts) is helpful.

The best treatment probably is correction of any endocrine change and removal of any focus of infection.

The course of the disease makes evaluation of the effectiveness of any treatment difficult.

BIBLIOGRAPHY

Texts:

Becker and Obermayer: *Modern Dermatology and Syphilology*, xii, 871 pp., Philadelphia, J. B. Lippincott, 1940.

Sutton and Sutton: *Diseases of the Skin*, Ed. 9, 1433 pp. St. Louis, C. V. Mosby, 1935.

Articles:

Baehr, G. and Pollack, A. D.: J.A.M.A. **134:** 1169-1174 (1947).

Beerman, H.: Amer. J. Med. Sciences: n.s. 216: 458 (1948).

Bernstein, E. T. and Goldberger, L. A.: J.A.M.A. **130:** 570 (1946).

Dostrovsky, A.: Arch. Dermat. and Syph. **55:** 1-11 (1947).

Dostrovsky, A. and Sagher, F.: Brit. J. Dermat. **58:** 52-61 (1946).

Duff, G. L.: Canad. M.A.J. **58:** 317-325 (1948).

Jager, B. V. and Grossman, L. A.: Arch. Int. Med. **73:** 271-285 (1944).

Keil, H.: Arch. Int. Med. **66:** 109-139 (1940).

Keil, H.: " " " **66:** 339-383 (1940).

McCombs, R. P. and MacMahon, H. E.: M. Clin. North America **31:** 1148-1162 (1947).

Norman, C. F.: Geriatrics **2:** 24-33 (1947).

O'Leary, P. A. and Waisman, M.: Proc. Staff Meet. Mayo Clin. **15:** 702-704 (1940).

Rothman, S. and Felsher, Z.: M. Clin. North America **31:** 198-212 (1947).

Vallee, B. L.: New England J. Med. **235:** 207-213 (1946).

Wells, C. A.: Bull. Acad. Med. Toronto **15:** 15-22 (1941).

Wuerthele, V.: J. M. Soc. New Jersey **44:** 52-53 (1947).

A PROBLEM IN DIAGNOSIS, PART II

T. A. McLENNAN, 5T0

DIFFERENTIAL DIAGNOSIS

PRIOR TO INVESTIGATION in hospital two possible diagnoses had been considered.

Subacute bacterial endocarditis occurring on a patent ductus arteriosus was suggested by chills, sweats, weakness, orthopnoea, mild pyrexia and slight leucocytosis. The murmur, however, was not characteristic and the chest findings could not be explained adequately.

Pericarditis with effusion may be associated with generalized weakness, malaise, chills, sweats, dyspnoea, low-grade fever and a pain similar to that experienced by the patient. The lack of venous distension, cyanosis and muffled cardiac sounds made this diagnosis less probable and the absence of a characteristic heart shadow on radiological examination eliminated it.

Having completed x-ray studies of the patient's chest, the problem in diagnosis became the determination of the exact nature of a mediastinal mass in a teenage girl.

Posterior mediastinal tumours differ from anterior mediastinal tumours because of the specific structures situated posteriorly. Tumours of nervous tissue origin, such as *neurofibromata* and *ganglioneuromata*, and *oesophageal growths* were unlikely possibilities after laminagrams had localized the mass to the anterior mediastinum. *Aortic aneurysm* was extremely unlikely from any cause. Isolated *tuberculous disease* of the mediastinum was ruled out by negative tuberculin tests and by the absence of changes in the lung fields.

The common masses encountered in the anterior mediastinum, in order of frequency, are lymphoblastoma, dermoid cyst, teratoma, thymus tumour, ectopic thyroid, lipoma and various cysts.

Lymphoblastoma usually grows rapidly in a lobular fashion, extending laterally to both sides of the mediastinum. Low grade pyrexia, anaemia and malaise favour *Hodgkin's disease* while a rapid clinical course suggests *lymphosarcoma*. A unilateral mass does not exclude either diagnosis, but makes both less likely. Regression in size resulting from radiotherapy in doubtful cases may be used as a diagnostic measure, but valuable time may be lost—making a previously operable lesion inoperable.

Dermoid cyst characteristically is a moderately dense, rounded tumour situated near the base of the heart. Lobulation is not characteristic. Calcium, in some cases, may be deposited in the wall of the cyst.

Teratoma, in this case, is the favoured diagnosis because of the onset near puberty and the slight pyrexia and leucocytosis. It commonly occurs in the same position as the dermoid cyst. Teeth or bits of bone may be seen in the x-ray. Positive Aschheim-Zondek tests may be found occasionally and are due to the inclusion of chorionic tissue.

Thymus tumour is not a likely possibility since it is usually found just below the substernal notch. Benign thymomata may be associated with myasthenia gravis; most thymomata are malignant and the signs and symptoms that they present are due to compression and invasion of mediastinal structures.

Ectopic thyroid may be found in this location. The majority of intrathoracic goitres give some indication of origin from the neck and the clinical picture

may sometimes be that of inspiratory stridor, paroxysmal asthmatic wheezing, brassy cough, and jugular distension. Calcification at the edge of a thyroid adenoma may aid in its recognition occasionally.

Lipoma is suggested by the relative translucency of the mass. The rapid clinical course makes liposarcoma a more likely diagnosis. Calcification can occur in the walls of a lipoma, but this is not very helpful as it may occur in any slowly growing, encapsulated mass.

Simple cyst may occur as a tracheal, pericardial or serous cyst. The rapid clinical course and the illness of the patient in company with the lobulated appearance on x-ray lends no support to this diagnosis.

Secondary tumour is unlikely in this age group. Silent primary conditions, such as Wilms' tumour and adrenal medulloblastoma, that can occur at this age, tend to metastasize via the blood stream and prefer to seed in the lung rather than in the mediastinum.

CLINICAL DIAGNOSIS

Malignant teratoma

TREATMENT AND CLINICAL COURSE

Although it was thought that the mass was probably malignant and inoperable, a thoracotomy was done in the hope that the tumour could be removed or, at least, a diagnosis could be made.

At operation on October 25, 1949 a spherical, encapsulated, anterior mediastinal tumour was found jutting into the left chest, displacing and collapsing the left lung. The mass was adherent to the pleura of the opposite side, to the great vessels and to the pericardium. After some difficulty a loculated mass $11 \times 8 \times 6.5$ cm. was removed intact. Following a stormy post-operative course the patient recovered completely. Microscopic examination of the mass revealed small chips of bone, cartilage, striated muscle fibres, connective tissue, and glandular cells resembling gastric mucosa. There was no evidence of malignancy after serial sectioning. The final diagnosis was *benign teratoma*.

ACKNOWLEDGEMENT

It is a pleasure to acknowledge the valuable assistance of Dr. R. M. Janes and Dr. W. B. Spaulding during the preparation of this case report.

REFLECTIONS UPON THE PROBLEM OF OBESITY

JOHN A. BESWICK, 5T0

"Healthy habits would become more prevalent if the consequences of their neglect were more immediate and invariable."

Sir Thomas Lewis[2]

DEFINITION

Obesity is a physical state in which there is excessive storage of body fat. There are many types of obesity, including rare varieties associated with metabolic disorders, painful fatty deposits or bizarre distributions of fatty tissue, but our chief concern here is the common type of obesity in which the patient is overweight but otherwise normal.

INCIDENCE

If moderate degree of obesity are to be included, this is one of the commonest afflictions of mankind. It is stated (1) that ten to fifteen percent over optimum body weight is the rule rather than the exception after the age of thirty, women being more commonly affected than men.

AETIOLOGY

The cause of obesity in all cases is a caloric intake in excess of metabolic needs. However, such a simple explanation does not expose the underlying reason for overeating. Some individuals have large appetites because of training; some resort to overindulgence in food as a result of conflict situations, anxiety, or as an expression of their appreciation of their environment. Others with normal appretites lead relatively inactive lives and store fat because of the imbalance between food intake and energy expenditure. Once the process of fat storage is established, there is a tendency for a person to decrease his activity and to have more time to think about satiating his appetite; a vicious circle is thereby established.

SIGNIFICANCE

Statistics have shown that there is a high correlation between obesity and premature death. Morbidity is high amongst the obese, the commonest illnesses probably being coronary heart disease, diabetes and hypertension. One tragic and often overlooked fact is that these people miss much of what life has to offer. The fat person stands out amongst his associates and neighbours. He is thought of, and thinks of himself, as a fat person. He is the butt of stereotyped jokes in which he often takes a good-natured part himself, but behind this laughing acceptance of his situation is often a sincere desire to be like other people. His physical activity is restricted in proportion to the degree of his obesity and, from time to time, he is painfully reminded of his limitations, as when he faces a medical examination for life insurance or when he is refused employment.

INFLUENCE OF SOCIAL FACTORS

The pattern of our culture is such that an individual is encouraged to become fat. As a child, he is impressed with the importance of eating; his parents know that nutrition is essential to his growth and development and so they believe that the child's health will be improved in proportion to the volume of his caloric intake. As he grows older, he is beset from all directions by advertising ma-

terial extolling the virtues of beautiful, tempting food. He attends parties and social functions where the central concern lies in loading up the stomach. Food is spoken of everywhere in endearing terms and nobody ever heretically suggests that perhaps this delightful boon may really be a threat to health and to life.

As he matures, with his table habits well formed, he learns of the use of alcohol which, being a liquid, is not considered as a food (seven Calories per gramme). He gets married, begins to lead a quiet life and takes up a sedentary occupation, but his appetite remains unchanged. The fattening process continues apace.

WHY ALL FAT PEOPLE DO NOT DIET

In view of what has been said, it seems strange that all fat people do not cut down their food intake and, in so doing, make themselves normal individuals. But there are certain mechanisms at work maintaining the old order.

When the question of diet arises, the obese individual has immediate fears of hunger. Having forgotten the feeling of normalcy, he refuses to measure the acute sensation of hunger, which he knows, against that nebulous state of well-being which he cannot fully appreciate. He does not understand the almost mathematical relationship between caloric intake and body weight, and so refuses to believe that the answer to his problem is as simple as a change in dietary habit. He tends to rationalize his gluttony by thinking of it as a necessary means of maintaining good health; he considers that he would be unable to carry on with his work if he should eat less, and that a diet would precipitate an illness. In this line of thought he is often aided by friends and relatives who "love to see a man eat".

Some fat people, particularly males, are proud of their weight, confusing a high scale reading with strength and health. Others are unduly afraid that a loss of weight would render their clothes unfit for wear; they do not seem to be quite so concerned that their present table habits may bring about the same result, in the opposite direction.

One point which causes obese people much concern, and which discourages them from taking active steps toward reducing, is the mental comparison they make between themselves and others. Having no true knowledge of quantitative differences in energy expenditure, metabolic activity, nor, indeed, in actual food intake, they think they see people all around them who eat more than they themselves do, and who do not become fat. Such "observations" are not conducive of a rational approach to the problem.

WHY DIETS ARE OFTEN ABANDONED

It is probable that most reducing diets fail in their purpose. There are many reasons for this, most of them based upon poor insight and a lack of understanding of the therapeutic value of proper diet. Many individuals commence to diet as a fad without a real determination to reach a definite goal. Some are readily discouraged by an initial failure to lose weight or by too slow progress; they want to be slim tomorrow, not six months from tomorrow.

In the matter of dieting, interference from friends and relatives is perhaps the rule. The fond mother or wife is prone to tell the reducing subject that he looks "terrible," "wan" or "peaked"; she frets when he refuses to take second helpings

as he used to do, and she expresses fears that he will become ill. If he does become ill, for any reason whatever, the diet is named as the cause and pressure is applied to have it terminated.

Many people are quite content to lose a few pounds rather than many. They start out as fat people, end up as stout people, and consider their efforts successful.

An appreciable number of dietetic failures may be attributed to excess initial enthusiasm. Instead of adopting a long-term plan, certain impetuous people will begin an eight hundred Calorie diet which leaves them ravenous; they soon find that losing weight can be an unpleasant affair and the plan is promptly shelved.

WHY SOME DIETING PEOPLE FAIL TO LOSE WEIGHT

There is only one reason for failure to lose weight; caloric intake is at least equal to metabolic needs and the stored fat is not mobilized to meet energy demands. The tendency seems to be for these people to eat additional food and to rationalize their behaviour to a marked degree. They may seem quite convinced in their own minds that they are adhering strictly to the diet, but the fact remains that a sufficiently low intake is inevitably followed by weight loss.

SUGGESTIONS REGARDING TREATMENT

Treatment should be directed at the basic cause. If there is evidence of anxiety or other reaction to environmental influences these problems must be met at the same time that the overlying symptom is treated.

Obesity is a chronic curable state which is best met by giving the patient a clear understanding of, and an interest in, his condition. The particular diet used is not important so long as it is acceptable to the patient and supplies adequate protein and vitamins without meeting the body's caloric requirements.

These patients are often quite receptive of factual information about this misunderstood condition. A little time spent with them explaining the mechanism of gaining and losing weight can make the difference between success and failure in treatment.

A definite goal should be set and nothing should be allowed to interfere with the attainment of it. The patient should have a set of bathroom scales; these are very important in holding the interest and they provide the only means by which progress can be closely followed. A good idea is to provide the patient with a sheet of graph paper marked off vertically in pounds and horizontally in weeks; this graph may be filled in by weekly readings made at the same time of day, wearing the same amount of clothing (preferably none). A warning should be given that there will not be a linear drop in the weight curve, and failure to lose weight in one week is not necessarily an indication that results are not being obtained. Observations made at different times in a single day may show a variation of three or four pounds, due mostly to changes in fluid balance.

Active interests should be encouraged. This does not mean that the patient is obliged to exercise in order to achieve his goal, but if he is occupied with time-consuming activities, he will have less time to think about his empty stomach. Parties and afternoon teas are a bad influence upon the dieting patient; if he is to succeed in his efforts, he should avoid the company of those who eat for

pleasure. It is not easy to keep saying "no," when it is so pleasant and socially acceptable to say "yes."

Exercise need not be prescribed unless the patient is exceptionally intent upon his purpose to reduce. For exercise, although it does increase metabolism, tends to stimulate the appetite with the result that the will to diet may soon break under the pressure of the desire to eat.

Most people do not understand the difference between "appetite" and "hunger". Hunger is a physiological sensation whose origin is in a relatively empty stomach, while appetite is a function of cerebral cortex and may be experienced even when the stomach is full. Those who eat more than they need often express the idea that it is right to continue eating as long as the thought or eating is pleasurable, regardless of the epigastric tension which results.

The difficult and important task is to convince these people that hunger is a good sensation, for, if it is experienced long enough, body fat will be mobilized and weight will be reduced. An enthusiastic practitioner can instil enthusiasm into his patient, teaching him that dieting can be a game and that sensations of hunger, rather than being bad, are an indication that progress is being made.

For the obese individual, the appetite is a completely false guide to optimum food intake; another guide must be found. Such a guide is the bathroom scales, by which caloric intake is reflected in weight gain or loss. Unlike a well calibrated appetite, however, it does not give immediate readings at each meal; its readings must be taken over a period of time, as has been pointed out above.

An important concept for the obese patient to grasp is that food in excessive amounts is, *for him*, a sort of slow poison. During the reducing process, this idea can be firmly implanted so that, once normal weight is attained, the patient need not resort to his former habits.

Adjuncts to diet, designed to decrease appetite or to increase metabolism should not be resorted to without serious consideration. They may help the patient toward his goal, but he is not cured until he can maintain normal weight unassisted by such artificial props. Since obesity has a strong tendency to recur, the patient will rapidly return to his former state if he stops using the drugs which have assisted him to lose weight. Thus, if they are used at all, they should be gradually withdrawn so the patient may learn to stand upon his own feet.

Finally, there is one principle in the treatment of obese patients which is sometimes overlooked: the impact of the practitioner's advice bears an inverse relationship to the degree of his own corpulency.

REFERENCES

Cecil, Russell L.: *A Textbook of Medicine*, Ed. 7, 1730 pp., Philadelphia, W. B. Saunders Co., 1947.

Lewis, Sir Thomas: *Diseases of the Heart*, Ed. 4, 304 pp., London, Macmillan and Co., 1948.

THE UNIVERSITY OF TORONTO
MEDICAL JOURNAL
(AN UNDERGRADUATE PUBLICATION)

FACULTY ADVISORS
E. A. Linell, M.D.
J. H. Couch, M.A., M.B., F.R.C.S., F.R.C.S.(C.)
J. Hepburn, M.B., F.R.C.P.(C.)
H. H. Hyland, M.D., M.R.C.P., F.R.C.P.(C.)
D. Y. Solandt, M.A., M.D., PH.D.
B. F. Crocker, M.A., PH.D.

CONSULTING EDITOR
W. G. B. Casselman, M.A., M.D.

EDITOR-IN-CHIEF
G. L. Ralph

ASSOCIATE EDITOR
D. C. Harrison

ASSISTANT EDITORS
D. E. Yates, B.A. D. J. Lewis, B.A.
R. L. Smith T. A. McLennan

EDITORIAL ASSISTANTS
I. A. Mitchell, B.A. W. J. D. Cooke
S. L. Wax Miss J. H. Griffin, B.A.
W. J. Kokeny

MANAGING EDITOR
R. M. Hines

FEATURES EDITOR
M. L. A. Auerback

ABSTRACTS
Editor: D. I. Gove
Assistant Editors:
A. Bernstein, B.A. F. Williamson
W. E. Sullivan

CIRCULATION
Manager: R. G. Leckey
Assistants:
A. Lowden W. N. Clark D. E. Boyarchuk

ADVERTISING
Manager: B. Berman
Assistants: G. V. Secord, Miss M. Sada

This journal is published six times during each session, between October and March, by the Medical Society of the University of Toronto, to serve as a medium for student expression and to bring to each student recent articles of scientific interest.

$2.50 per volume. **50c per copy.**

Authorized as Second-Class Mail
Post Office Department, Ottawa

EDITORIAL

HALF A CENTURY OF MEDICINE

At this time, half way through the twentieth century, it is interesting to review the last fifty years of medical progress.

In 1900, medicine had barely grown into a science. Its rapid advance since then is due to at least three factors. Firstly, there has been a greater application of the scientific method, both directly and indirectly, to medical problems. Secondly, two great wars have stimulated all scientific endeavour. Thirdly, faster and more efficient methods of communication between co-operating scientists throughout the world have developed.

Osler,[2] in *Principles and Practice of Medicine*, Edition 2 (1897), discussed most of the diseases recognized today. Although he usually painted the clinical and pathological pictures of diseases accurately, his paragraphs on aetiology and therapy do not apply today. Written in the great era of bacteriology, long sections were devoted to descriptions of causative organisms and whether or not they satisfied Koch's postulates. The successful treatment of myxoedema by oral administration of thyroid extract was hailed as a triumphant therapeutic advance.

At that time, physiology, in comparison with the subject it is today, was primitive; pharmacology was mainly a study of empirical recipes; the biochemist and the clinician tended to regard the results of each other's work with mutual distrust; endocrinology was unknown.

Today, following the discoveries of many new aetiological agents of disease and triumphs in treatment, and because of better public health measures, a vast change has come over the scene of

medicine. Insulin, liver extract, cortin, cortisone, diphtheria antitoxin, the sulphonamides, penicillin and other antibodies, vitamins and other specific nutritional adjuvants and DDT have miraculously meant life to millions. New and improved methods of diagnosis—by x-ray, chemical analysis, electro- and angiocardiography, for example, and amazing advances in all forms of surgical technique, including cardiovascular, thoracic, brain and bone surgery have aided greatly in expeditiously returning patients to health.

Many changes have occurred in the field of medical practice in fifty years. In 1900, the general practitioner predominated throughout the country. He was respected and loved by a complacent community. His practice was simple—nearly all laboratory tests could be performed at the bedside and therapy was chiefly empirical. He often practised with the confidence that all possible was being done for the patient.[3] Although he may not have realized it, his art was often a more effective means of therapy than his science. His office expenses were low, for the multiplicity of diagnostic equipment now available had not been developed. The cost of illness to his patient was lower too. Except for surgical cases, private hospital rooms were used rarely and even these cost only a fraction of what one pays for ward accommodation today. The relatively expensive present-day diagnostic procedures of the laboratory and x-ray were not used. Difficulties in transportation tended to cause the practitioner to settle in one place and stay there. There were no fast rail, highway or air services to facilitate frequent trips to large medical centres for refresher courses and conferences. Specialization was practised only by a few men in teaching centres and large cities. Only within the last 25-30 years specialism has risen with its tendency to consider the component part rather than the whole patient.

What changes occurred in the teaching of medicine in the first half of this century? Obviously, today's student is confronted with a vastly greater amount of medical material to learn than that which faced his counterpart of 1900. Aiding the present-day student, however, is the more logical and orderly presentation of his subject. With a more complete understanding of the workings of the body and a wider knowledge of the aetiology of many diseases it is easier for him rationally to understand and learn the clinical picture and treatment of diseases. He also is aided to some extent by technical advances, such as colour photography, sound films and, recently, television. Today's medical student, however, studies at least twice as long as his predecessor of 1900 did, between high school and his entrance to medical practice.

But what of the future? That medical science will continue to advance, unless nations take the road of atomic warfare to collective and total suicide and the destruction of human society, no one doubts. Present-day discoveries and research suggest the direction in which the most significant advances will be made. The therapeutic properties of cortisone and ACTH are not fully explored. Cancer research undoubtedly will yield some fruitful results. The use of radioactive isotopes, of new antibiotics and of hormones probably will change the courses of many diseases. The discovery of atomic fission,[4] the groundwork for which was laid at the beginning of this century, presents two

great challenges—the bending of it to usefulness and the guarding of people against its deleterious effects; its prophylactic, therapeutic and diagnostic potentialities well may result in the solution of some of medicine's most formidable problems. The large-scale research through which the first atom bomb was created has shown that through scientific teamwork great achievements can be made; if such combined efforts are carried on in future the resulting benefits to humanity should be very great.

With its ever-increasing bulk and intricacy, medical science is becoming more and more difficult to assimilate completely by student and practitioner. For this reason it probably will be necessary and desirable, in future, to provide the medical student with greater freedom in the choice of subjects within the medical curriculum, so that his own special talents can be used to best advantage in the broadening field of medicine. It seems unlikely, however, that specialists ever completely will replace general physicians for, as McMichael[1] has pointed out, there are three reasons for confidence in the future of general medicine. Firstly, there is the integrating influence of physiology in medical teaching. Secondly, the prolongation of life is shifting the age distribution of the population so that the frequency of combined diseases is increasing. Finally, the need for specialists who rely on skill in particular techniques will steadily decline in the face of broad therapeutic advances.

The recently formed World Health Organization, dedicated to the aim of a physically, mentally and socially healthy humanity, realizes that time and distance have been wiped out in recent years and that public health has become the concern of the whole world. The steps it is taking toward control and eradication of malaria, tuberculosis and venereal, pestilential, parasitic, virus and other diseases; coupled with its attempts to improve environmental sanitation in the underdeveloped areas should do much to improve world health generally during this half century.

As medical students we should be thankful that we are privileged to witness and participate in the great medical achievements of this age. Let us resolve, however, to remember always the words of Leplace:

"What we know here is very little, but what we are ignorant of is immense."

REFERENCES

(1) McMichael, J.: Canad. M. A. J., *58*, 84-89 (1948).
(2) Osler, W.: *The Principles and Practice of Medicine*, Ed. 2, xviii + 1143 pp., New York, D. Appleton & Co., 1897.
(3) Palmer, W. W.: Diplomate, *21*, 247-254 (1949).
(4) Pugh, H. L.: *ibid.*, 284-288

RHODES SCHOLAR

The Staff of the JOURNAL, along with the entire Faculty of Medicine, extend heartiest congratulations to Bob Hetherington, the fourth medical student* at This University to be elected a Rhodes scholar. Bob has amply displayed, by his brilliant academic record, his vigorous leadership in student organizations and his energetic and successful participation in athletic activities, the distinctive qualities necessary to win this great honour.

It is our belief that Bob's achievement is, for him, but one more step toward those realms of Medicine in which only truly great men tread.

*Other Rhodes scholars who attended This Medical School are W. Hurst Brown (1921), K. A. Hamilton (1921), Dean J. A. Macfarlane (1922), H. R. Ziegler (1929), F. G. Kergin (1930), and J. W. Magladery (1934). Not all of these men, however, were in attendance at medical school when the award was made.

FEATURE

WRITING BETTER EXAMINATIONS

J. V. BASMAJIAN, M.D.*

THERE SHOULD BE NO NEED for apologizing for either the title or the content of this essay. Every few days I am approached by another student with the plaintive query, "How should I answer examination questions?" Having recently marked a set of Anatomy term papers, and with that memory fresh, I shall attempt an answer in writing. It should be taken for granted that what remarks I have to make are applicable to the writing of examinations in *any* subject, and, since most of us will encounter written tests of one sort or another for years to come, it may repay even the honour student to spend a few minutes in consideration of the art and science of the written answer.

First of all, it is obvious that you, the student, must have a reasonable grasp of the subject of the examination. No amount of "system" is going to help you pass if you have not studied properly or if you just do not have the required amount of cerebral cortex or connector pathways. (Incidentally, a book that covers the study angle admirably is "Doctor in the Making" by Dr. Ham and Dr. Salter. Indeed, they probably discussed examination writing as well, but I shall not renew my acquaintance with their excellent book for fear of plagiarizing it.)

Let us take for granted, then, that your I.Q. is adequate and your study methods good. Why do you not get better marks? One very good reason may be that you approach an examination with the deplorable attitude of fear and dismay rather than with confidence that you are going to do as well as you can. If more students would approach the examination hall as though they were going to a straight race rather than an obstacle course there would be less hysteria and better results. Nothing is better for putting all your faculties at peak pitch than the adrenalin-excitement preceding the former situation. Even the best candidates are all keyed up—perhaps even more than the poor ones. The man who thinks the examiner is "out to get him" is foolish and can never give of his best. What pitfalls there are, are of his own making, and the only obstacle worth a thought is ignorance.

Even before entering the examination room *you* can contribute to greater success. A few rules, religiously observed, will prove worthwhile. Never (yes, never) cram to the last minute, unless of course, the professor has just told you on the bus coming down to school exactly what is going to be asked—a very unlikely occurrence. Last minute cramming seldom covers the subject and simply pushes knowledge assimilated earlier and more painstakingly into more inaccessible crannies of the mind.

BE ON TIME, preferably early, so that you can make calm preparations. The 5 minutes preceding the examination should be spent not in frantic discussions with your neighbours, but in simple worthwhile tasks such as reading the instructions on the answer book, filling

*Lecturer in Anatomy, University of Toronto

in name and other requirements, making sure that your time-piece is synchronized with the clock and that all your writing equipment is ready. If you have an extra fountain pen bring it with you, filled and ready for emergencies. For some as-yet-undiscovered reason more fountains pens run dry during examinations than during any other period. Have a black pencil and a ruler and if margins are lacking draw them while you are waiting to begin. A few coloured pencils may prove useful in almost any examination.

By the time you have made your preparations the question papers will have been distributed. The first thing to note is the total allotted time as compared with the number of questions. So many students go wrong on this point that I would suggest that you actually spend 20 or 30 seconds working out on paper how much time you are going to spend on each question, bearing in mind the individual mark-values. Then you must OBEY THE CLOCK or you are sure to lose marks.

Some self-styled authorities assert that you should read over the whole paper first and decide the order in which you wish to answer the questions. Being a self-styled authority myself, I would suggest that in the long run this may prove to be as much a hindrance as a help. There should be no hard and fast rule, and you may find that taking the questions in order, one at a time, and with the clock in mind, is easier and less nerve-wracking. If, however, a *choice* of questions is given, you must decide early which ones you choose to answer and which to omit. From my own experience I would judge that such a choice is usually quite painless.

With all these more or less mechanical preliminaries out of the way we come to the actual answers. Here I join the throng of teachers who cry with anguish, "PLEASE, READ THE QUESTION CAREFULLY AND, PLEASE, ANSWER WHAT IS ASKED." The conscientious examiner has gone to great pains to make the question as clear and unequivocal as possible and feels hurt when some students appear to be confused. Eventually, it hurts the students too, needless to say.

There is neither room nor justification for "PADDING" an answer. Not only is this a patently transparent device that would not fool a child, but it wastes valuable time. Let alone the fact that in most cases it will not garner extra marks, in some cases it will actually lose marks already made! Perhaps we should classify IRRELEVANCE with "padding" since it has the same value. If you are asked to *name* a certain group of muscles (or diseases, or symptoms), you will receive no credit for giving detailed descriptions. On the other hand, if a description is called for, a list of names is not enough. Wandering far afield from the subject under discussion is a temptation that must be avoided scrupulously. For emphasis, I repeat: AVOID PADDING AND IRRELEVANCE.

A SYSTEM OF ORDERLY THOUGHT will not only impress the examiner favourably but will, *pari passu*, bring about a more complete answer. Why impress him favourably? A brief consideration of how marks are earned will be answer enough. Most markers bear in mind what the requirements are for a "pass" and for "honours," 50% and 75%, in most subjects. An orderly, systematic presentation certainly will be a criterion for whether the answer is to receive a pass or an honour mark instead of coming just "below the line." *You* do the passing or failing or the getting of

honours; the examiner only acts as the judge or referee. Consciously or unconsciously, examiners definitely make allowance for *bonus marks* and such bonuses are well worth the effort.

As with most students, you may find it advisable to gather your thoughts by jotting them down in the form of a rough plan on the unruled opposite pages set aside for this purpose. A minute or two, so spent, will increase the yield by ten per cent or more. It is almost a truism that orderly thinking on examinations will carry over to orderly thought at the bedside of future patients.

In the simple chore of putting down on paper what you know, you can either earn or lose marks easily. Always put the QUESTION NUMBER prominently in the margin since most tests are marked by a team, of which each member is responsible for one question. If it takes a minute's frustrated hunting for the examiner to find your answer to the question he is marking, you will not deserve his charity. It follows, too, that when your answer is continued on another page, say so and on what page. Numbering the pages will prove worthwhile in such circumstances (see figure 1).

HEADINGS AND SUBHEADINGS, appropriately underlined, will give a better appearance and greater clarity. A system of INDENTING subheadings and the subject matter that follows is generally advisable even with subjects of abstract discussion (see figure 1). If you are allergic to headings (although most examiners are not) the least you should do is break up your answer into appropriate sections or paragraphs. It may even be wise to leave 2 or 3 lines between paragraphs and 5 or 6 lines after the answer to each question. After-thoughts can be added at appropriate points without jamming them in between lines and causing confusion.

Certain subjects lend themselves to the simple expedience of "MAKING POINTS." Whenever you resort to this method you should beware of making a meaningless hodgepodge. To be safe, *avoid* point-making except where it is called for especially, and use sentences wherever possible, even though they may be rather gaunt and ascetic. Only the extraordinarily well-informed person *must* and *can* resort to a skeleton presentation successfully. The average student is in danger of making his presentation more like a box of unrelated bones if he leaves out the "meat" of verbs, pronouns, and infinitives. The examiner, after all, is not a technician or a clerk with an adding machine, but is a competent judge, who must consider your answer qualitatively as well as quantitatively. He may resent having to articulate a widely-strewn skeleton of an answer. On the other hand, avoid the opposite extreme of verbosity which takes time and is of no value. If you must develop "the grand bed-side manner," please, don't practise it on your instructors.

DIAGRAMS, too, are often valuable. If you want marks for them make them large and accurate; caption them (*e.g.*, "Anterior view of wrist joint") and label the parts. Colour, judiciously employed, is usually helpful. If you are poor at diagrams do not waste your time at them unless they are in rough on the opposite pages and are only for marshalling your thoughts.

Perhaps most of what has already been discussed has seemed obvious. If so, the next part will seem even more ridiculously apparent. POOR WRITING can create the poorest rapport possible between the student and teacher. How

(page) 6

3.

(a)

(b)

(c)

* NOTE: Continued on p. 14, Book II.

FIG. 1.—A sample of good "lay-out". Note page number, question number, headings, sub-headings, appropriate indenting of sections and underlining. The writing is atrocious, however.

can any examiner remain completely objective and rational when he is confronted by an illegible mess? (see figure 1).

I would estimate that good writers (*i.e.*, legible writers) receive 4 to 5% more marks for equal knowledge than their more careless brothers. I refuse to believe that the majority of poor writers of college age cannot improve. Even the poor writing of prescriptions by older physicians is usually an affectation which has become ingrained.

Another deplorable example of carelessness is POOR SPELLING, especially in technical words. Seldom is it justified. Care also should be taken that SLIPS, such as writing "medial" when "lateral" is meant, are avoided or corrected. This brings me to the point that there should always be a few minutes at the end of the examination devoted to going over the answers, correcting such slips and improving the general appearance of the paper.

Finally, let me point out what I think is the worst violation of the rules of good answers. This is the all too common practice of taking too much for granted, *i.e.*, assuming that since the examiner must know all the simple, "obvious" points, he wants to hear of the more exotic ones only. It is necessary for you to demonstrate your knowledge and not to rely upon the marker's guesswork. For example, in a discussion of Biceps Brachii, it is not enough to say only that the insertion is the biceps tuberosity. That is about as useful as saying that the Pennsylvania Turnpike is in Pennsylvania. Of course the examiner knows the location of the tuberosity and where on the tuberosity the tendon is attached; but have you shown that you do too? Therefore, a good system to use is to assume that the examiner will accept only what you put down, and that you are writing a DEFINITIVE ARTICLE FOR HIS EDIFICATION. If you keep this in mind and follow the suggestions made in the preceding paragraphs you cannot fail to improve your results.

ACKNOWLEDGEMENT

In the preparation of this article many friends and colleagues, particularly Professors Grant and George, gave valuable advice for which I am very grateful.

HUMANISM AND MEDICINE

H. B. VAN WYCK[1]

PART X

MEDIAEVAL MEDICINE AND ITS AGE

THE MEDICINE OF MEDIAEVAL Western Christendom which included Italy, France, England, and Germany, may be summed up as a corrupted version of Galenism. Dr. Singer, an eminent historian of science, passes on from the death of Galen, 199 A.D., to write: "The Dark Ages for medicine have begun." From then on mediaeval medicine was characterized by an almost complete absence of patient observation without which, and the resulting hypothesis and experiment, science always becomes static. Those who wrote on medical subjects, largely monks, were content to copy, often inaccurately, the older records. When the citation of authorities meets all requirements, science is unproductive. The true scientific tradition by the 4th century was almost lost in the west, and its revival did not begin until the 12th century, and until, from the more progressive Arabian culture in Spain, translations from the older medical works stimulated the west to a rebirth of interest in medicine and its basic sciences.

It must be noted, however, that with the advent of Christianity into the Mediterranean world the profession of medicine received an ethical impulse which it has not since lost. There does not appear in the ancient pagan Mediterranean world that sense of duty which compels service, unremitting and unrewarded, to the unfortunate, a function which, however dim became the scientific scene, has remained the proud badge of western medicine. The ideal of service to one's neighbour being as important as the worship of God was the inestimable gift of Christianity to the art and science of medicine. Meagre as are the records, there is no doubt that as early as the first century, a changed point of view revolutionized the care of the poor and the needy. This was seen in the development of hospital organization. The Roman, whose organizing genius gave much to the west, made one great contribution to medicine—the hospital system. By the time of Augustus, the valetudinaria were established in army camps and also attached to each prosperous estate. These valitudinaria cared for soldiers, sailors, gladiators and slaves. "The solicitude of the pagan Roman for these all-important members of the Roman state was dictated not by a real sentiment of good feeling towards them as individuals, but by the perfectly comprehensible interest of a careful master who could not allow his property to deteriorate."[3] The philanthropic hospital where the poor are treated gratis if need be was a definite contribution of Christianity without parallel in any other epoch of human development. Between the pre-Christian and post-Christian care of the sick there was this great contrast, that love and service towards one's neighbour were regarded as Christian duties no less

[1]Head of the Department of Obstetrics and Gynaecology.
[3]Revillout, No. 78, p. 18.

than love toward God. Christ had said "I came not to be ministered unto but to minister." Of this the oft-quoted remark of Hippocrates, "Where the love of man is there is also the love of this art," is but a pallid premonition. The parable of the good Samaritan gave a programme as well as a gospel and the assurance, again an astounding change from the ritualistic demands of previous religions, "Inasmuch as ye have done it unto the least of these my brethren, ye have done it unto me," was a challenging invitation for service to common humanity, and lifted at once the exponents of Christianity and the nursing and medical profession to a new dignity and office. To tend outside the narrow limits of one's own home others in loneliness and distress became an avowed duty, and was expressed in the New Testament by the word *diaconein*, which is translated in the St. James version "to minister" or "to serve." These words at their highest have both a material and a spiritual sense and express the dualism of body and soul which again is essentially Christian. With this concept of service grew up the diaconate orders, the deacons and deaconesses, and it is again one of the joint glories of Christianity and medicine that the word "service," which at first referred to the work of slaves, became a badge of honour of the free men and women that devoted themselves to the sick and the unfortunate.

It is illuminating to find that the early hospitals devoted to the *diaconia* of the needy were called *Xenodocheia* or "Houses for the Stranger." These asylums made little distinction between the sick, the aged, pilgrims, or orphans; in these refuges, which took the place of our modern hospital, hostel, infirmary, and orphanage, anyone needy or unfortunate was an object of this charity. Hospitals only for the sick were not separated out as such until the 12th century. By the 5th and succeeding centuries, the public hospitals passed under the administration and protection of the monasteries and there were developed the orders of religious men and women who undertook the care of the inmates of these *Xenodocheia*—the military nursing orders or Knights Hospitallers, the secular orders, such as the Tertiaries of St. Francis, and the regular monastic orders. That these hospitals were ecclesiastical rather than medical, for care rather than cure, for the relief of the body if possible, but predominantly for the saving of the soul, does not obscure the fact that Christianity had endowed Western medicine with the pure and simple precepts of the new Testament. But, although faith and love were present, skill and science were often absent. That the long period of scientific stagnation was partly due to a reactionary Church may be regretted, but the spiritual domination of the Church over science may prove at long view to be no worse than the materialistic domination of science over the spirit of man. Either is a negation of freedom and the worth of the individual which it has been both the glory of Western medicine and Christianity to assert. If man receives the opportunity to progress from his present state the experience gained in the last twenty centuries should help to guide him in the perennial interdependence of his religious and scientific development. The tragedies of the first two millenia of the Christian era, the wars, some dynastic, others alas religious, the division of the West into a myriad points of disunity, the strife between the church jealous of science because blind to hard, stubborn facts, and science often contemptuous of the

Church because unaware of its own limitations, all this should in present-day enlightenment forever disappear.

However, if the precepts of the New Testament influenced a deeper humanity in the care of the sick, the Hippocratic tradition was for centuries ignored. Little or no scientific use was made of the clinical material and during these centuries, little advance was made in anatomy, physiology, or other branches of medicine. The monasteries, however, did preserve a slender thread of tradition and some of the ancient writings from Greek, Latin, and Arabian sources; and, when medical centres for teaching and practice began to emerge after the Dark Ages, they are found in the earliest stages of their growth developing in the shelter of monastic protection. The earliest and most famous centre was the Benedictine monastery of Monte Cassino near Naples, a monastery which had been founded by St. Benedict himself in the 6th century. Shortly after, it was sacked by the barbarian Lombards; rebuilt in 720, it was destroyed again by pirate Saracens in 884. Seventy years later it was restored and became the most famous monastery of the Middle Ages. In 1866, when such institutions were dissolved in Italy, it was spared, largely through English influence, and was preserved as a national monument with its monks as custodians. Then, again, history, as so often in the past, plots a master stroke of cynical recurrence. During the last war this precious old relic of the 6th century was destroyed again by a revisitation of the barbarian Germanic peoples.

The importance of the monastery of Monte Cassino is that it fostered the development of the university and medical school of Salernum. Thirty-five miles south east of Naples was the city of Salernum, to-day called Salerno; and, here in the ninth century close to the monastery of Monte Cassino, the monks organized what might be called the first university of modern history. This city of learning reached its zenith of influence by the 13th century; and then gradually became overshadowed by the other university centres of Boulogna, Padua, Paris, Montpellier, Naples and Messina. Its chief rival became the University of Naples and from the 13th century Salerno continued to lose standing. One of the last tokens of respect it received was in 1748 when the Faculty of Medicine of Paris referred to the Faculty of Salerno the subject of the relative standing of physicians and surgeons in France. In 1811 the medical school of Salerno was formally extinguished by a decree of the ruthless Corsican, the Emperor Napoleon.

To-day a visitor to Salerno would find no trace of the medical school which had once been its glory. Amidst the devastation of the last war, he would find no stone of the ancient edifice, not a manuscript in a library, no echo of tradition, not even a worthy reminiscence among the townspeople.

The University of Salernum owed its rise to eminence in part to its situation among the Greek colonies of southern Italy. Greek influence then as now was an important factor in stimulating educational development. At no time during the Middle Ages was Greek entirely a dead language in southern Italy and there were always Greek travellers and Greek sailors in Salernum and its neighbouring cities. Two other circumstances fostered the growth of the medical school at Salernum. The Benedictine monks from the beginning of the Order had a school in town and were always closely in touch with their great

mother institution in the nearby monastery on Monte Cassino. These Benedictines imparted an academic atmosphere to the town and gathered together the University which gradually came into existence about their school of Medicine. In addition, the equable and sub-tropical climate of the region favoured the development of the town of Salernum as a health resort to which patients flocked from all over Europe to enjoy its favoured weather and medical facilities. By the 9th century the Benedictine Hospital at Salernum was famous throughout the West. The students of the medical school, according to a law of the Emperor, Frederick II, in the 13th century, were required to spend four years in University before studying medicine, after which on the completion of four years in medicine, they had to pass an examination to gain the degree of Doctor, or a teacher of medicine. Before the recipient of the degree was allowed to practise himself, it was required that he spend a year of apprenticeship with a physician. This requirement of training at least in length of time, represents a high standard that soon was to lapse for hundreds of years and was regained only in the last century. The oath that was required on graduation was as follows: "Not to contradict the teaching of the College, not to teach what was false or lying, not to receive fees from the poor even though they were offered, to command the sacrament of penance to his patients, to make no dishonest agreement with the druggists, to administer no abortifacient drug to the pregnant, to prescribe no medicament poisonous to the human body." Such and oath revealed an ethical level that was higher than the scientific.

The formal name of the school at Salernum was *Almum et Hippocraticum Medicorum Collegium*. The most famous teacher was Constantine Africanus, who arrived from Carthage in about 1066, with the works of the great Arabians, Rhazes and Avicenna, whose work had preserved through the darkest centuries much of the best of Greek science. Constantine by translating these into a very poor brand of Latin, was the herald of the revival of learning that Arabian influence brought to the western world. The most famous text books associated with Salernum were *The Surgery of the Four Masters of Salernum*, a sort of combination work such as may emanate from a teaching centre of the present day, and *Regimen Sanitatis Salernitanum*, a code of health of the school which remained popular in Europe with numerous editions in circulation after the invention of printing. Salernum became a sanctuary and seminary for students and was the centre of medical studies until the Renaissance. "If we take up now the accomplishments of the School of Salerno in the different departments, there is one thing that is remarkable. It is the rich, independent productivity with which Salerno advanced the banners of medical science for hundreds of years, almost as the only autochthonous centre of medical influence in the West. One might also say that it was like a *versprengten Keim*—a displaced embryonic element—which, as it unfolded rescued from destruction the ruined remains of Greek and Roman medicine."[4]

After Salernum the next great medical school to develop was in Montpellier in southern France. Patients flocked to it as a health resort; and, among the numerous physicians who were attracted by its popularity, a medical school developed in the 10th century. As Mont-

[4]"Handbuch der Geschichte der Medicin"—Puschmann, Berlin, 1902.

pellier was not far from Marseilles which had originally been a Greek colony and maintained a strong Hellenic tradition, Montpellier is another example of the quickening of the artistic and intellectual life by a persisting Greek influence. Among the students were many from the British Isles, the Netherlands, Germany and, of course, Italy and France. Pope Innocent III summoned from Montpellier a member of the Order of the Holy Ghost, Guy of Montpellier, as one who would be best fitted to organize a model hospital in the Eternal City. Guy had built a great institution at Montpellier and on this model of the Hospital of the Holy Ghost many were the hospitals built by the Church throughout Christendom. Other famous graduates of Montpellier in the 12th and 13th centuries were Guy de Chauliac, Arnold de Villanova, Gilbertus Anglicus, and John of Gaddesden. Other schools soon appeared in Boulogne, Paris, and Padua.

Just as the Church took under its protection the hospitals, she exercised a more or less even jurisdiction over all the universities. What was taught in the classroom was regulated by her edicts and the books to which the students devoted their attention were chosen by ecclesiastical authority. By these means, during the Middle Ages education, especially in medicine, tended to be unpractical, theoretical, and dogmatic. In the lecture room after the recitation of a feeble translation of a Greek or Arabian author, the lecture consisted of the professor's comments on the citation. Anatomy had degenerated in all the old universities. The statutes of Montpellier prescribed "anatomy" at least every two years. These "anatomies" were held periodically and lasted several days. They consisted in the opening of the body cavities of the corpse of a condemned criminal by a surgeon while the attending professor gave a description of the contents. This deficiency in the teaching of anatomy by dissection was not overcome until about 1300; and not until Sixtus the 4th (1471-84), did any Pope permit dissections. However, at Boulogna and Padua, which were the least theological among European universities and where the dominant faculty was Law, regular dissections began to be practised early in the 14th century. "As the main beginnings of practical anatomy in the Middle Ages were due to the legists, so its finest performances, beyond all comparison, were due to the Renaissance artists and sculptors, in their struggle for perfect representation of the human body. Not until the epoch-making Vesalius, who comes just outside our period, was any medical work illustrated with figures even remotely comparable in accuracy of detail to the studies of Verrocchio, Dürer, Michael Angelo, Raphael, and, above all, Leonardo da Vinci."[5]

Until about the 10th century, surgery found no place on the curriculum of a university, and students of the art sought the tuition of private teachers and the wisdom of the ancients in manuscripts infrequently available. Even after 1300 the Paris Medical Faculty opposed the teaching of surgery and forbade its graduates to practise manual operations. At the College of Surgeons in Paris it was not until 1634 that the medical students could follow a course in surgery. This was given only in Latin. Thus, until the end of the period, the technical surgeons, the barber surgeons, remained outside the exclusive university groups and Lanfranc could lament that "Our pride in these present days

[5]G. G. Coulton—"Mediaeval Panorama."

(1280) hath left the office of phlebotomy to barbers, though of old it was the work of doctors, and especially when surgeons exercised that office." There was no clinical teaching as we understand it in any of the universities, the instruction being almost entirely oral dissertations in which ancient authors were read and commented upon, and to the theologians may be attributed an influence inimical to the advance of medicine at this time. The dry remark of Chaucer concerning his Doctour of Physike: "His study was but little of the Bible," is a commentary on the relation of theology and medicine during the earlier mediaeval times. By the end of the period, however, the Church had made important developments in the hospital system beyond anything that pagan Rome had known, and these hostels for the sick, the poor, the aged and infirm were in the later centuries a beneficent feature of mediaeval life, and as such, maintained an influence and tradition which ultimately was to nourish the reviving interest in a more scientific study of the body.

In general, medical care and sanitation in this mediaeval world was only rudimentary and paralleled the general standard of life. Paris and London before 1,000 A.D., were built of crowded hovels with straw on the floor and a hole in the thatch to release the smoke. The unpaved streets were quagmires and unlighted; no sewers; few schools; and only filth, mud, and pestilence lurking everywhere. In the words of one to whom the retrogression from the material comforts available to the privileged classes of the Graeco-Roman world would appear to be the total picture, and to whom the precedence given to spiritual and moral values by mediaeval Christendom does not weigh in the balance: "The Europeans were content to wallow in the mire—and dream of heaven. They were covered with hair shirts and vermin, but they prayed for purity of soul. They fought and robbed and murdered in the name of the Galilean. They scratched their tiny fields with a wooden plow, and their finest equipage was an ox-cart. Four oxen were a sign of royalty and as they shambled through the mud, the peasants humbled themselves. Their religion was as sombre as their words except when they decked themselves in flowers and celebrated pagan rites, not always chaste.

"They knew nothing of mathematics, of geography, of medicine, of astronomy. When one says nothing one means nothing. Of mechanics their knowledge was primitive. They knew the lever and the wheel and the pulley. But in all Europe, outside of Spain, there was not a man who could explain the principle upon which these devices worked. Not a man. Worldly wisdom was despised as something that might get between one and one's God. Ignorance and its son-Brutality, rules the human brain.

"Then came the crusades—those monstrous nightmares that troubled the religious dreaming of a childish people. They were frightful but they were cleansing. They served a purpose, though not the one for which they were intended. They curbed superstition, they broke down intolerance, they lessened the dread of religious authority, and they spread vague but insistent inquiries into the why of things. In a word, they ended the century-long sleep and the crusaders returned bitter and disillusioned—and awake.

"The minds of men were ready, or almost ready for the truth. And the truth-tellers were at hand."[6]

[6]"The Human Side of Science"—Grove Wilson, 1929.

It cannot be denied that the belief that the Bible, supplemented by Aristotle and Galen, contained all knowledge played its part in the delay of the progress of science for one thousand years, that as a result, Europe at times became a cesspool reeking with contagion, with plague-ridden cities laid desolate, and that the learned classes, the clergy in particular, were content of necessity to be more ignorant of natural science than is a ten-year old boy of to-day.

On the other hand, that earnestness in the search for spiritual values, that sense of unity under moral authority of the young embryo nations of Europe, and that devotion, often mistaken and more often frustrated, to the *ignis fatuus* of impractical idealism—all these were in synthesis a goal, the vision of which has become dim to the modern world. Of this, the Gothic cathedrals of Europe remain an arresting symbol. The recovery of that lost unity and that mediaeval emphasis on values is essential to man's happiness but when that loss shall be made good lies hidden in the uncertain future.

RECENT ACCESSIONS TO THE MEDICAL READING ROOM

Bovet, D. and Bovet-Nitti, F.: **Structure et activité pharmacodynamique des médicaments du système nerveux végétatif.** 1948.

Canada, Statistics, Dominion Bureau of. Health and welfare division: **Health reference book, 1948**. 1949.

Castiglioni, A.: **The renaissance of medicine in Italy.** 1834.

Congress de Chimie Biologique, 7th, Liège, 1946: **Un symposium sur les protèines,** par A. Tiselius, *et al.*

Kelly, E. C.: **Encyclopedia of medical sources.** 1948.

New York Academy of Sciences: **Thyroid functions disclosed by newer methods of study,** By J. H. Means and others. 1949.

Paré, A.: **oeuvres completes;** ed. by J. F. Malgaigne. 3 v. 1840-1841.

Sinai, Nathan: **Hospitalization of the people of two counties.** 1949.

Voegtlin, C and Hodge, H. C. (eds): **Pharmacology and toxicology of uranium compounds** 2 v. 1949.

Zilboorg, Gregory: **The medical man and the witch during the renaissance.** 1949.

ABSTRACTS

MEDICINE

Evidence Relating Life Situation and Emotional Response to Peptic Ulcer. Stewart Wolf, Annals of Internal Medicine, **4:** 637-648 (October, 1949).

In studies on a fistulous subject, by direct observation of gastric mucosa, by simultaneous collections of gastric juice, and by recording motility, by intubation with a balloon attached attached to a kymograph, the author and associates noticed the hyperfunctioning state could be induced by situations engendering anxiety associated with feelings of hostility and resentment. They also noted the stomach under these conditions was hyperaemic, turgid, and engorged. Furthermore, in the absence of ulceration, but in the presence of sustained hyperaemia and hyperfunction of the stomach, the characteristic ulcer symptoms of epigastric pain relieved by food or alkali, were frequently observed.

Gastric hyperfunction associated with sustained conflict also was attended by increased fragility of the mucosa and resultant erosion and bleeding points. They believe such erosions in contact with acid gastric juice effect a further stimulation of acid secretion, and suggest this as an explanation of the persistent hyperacidity often found in persons suffering from gastritis and peptic ulcer.

Opportunity was afforded to observe the gastric mucosa of a patient with a Brown-Buerger cystoscope, before and following vagotomy; during anger, aroused after surgery, the mucosa did not become engorged. The author cites further such observations from other workers.

Further data adduced from other patients with peptic ulcer, supports the view that peptic ulcer may be caused by sustained gastric-hyperfunction, which in certain individuals is an expression of their habitual reaction to stress.

The author believes the most fruitful information lies in a study of the way in which the individual habitually meets threats and challenges in his life situation, and what the implications of that pattern are for his health and survival.

J. A. Harbinson

Clinical Syndrome of Occlusion of the Posterior Cerebellar Artery, Levine, Cheskin and Applebaum, Arch. Int. Med., **84:** 431 (Sept., 1949).

The posterior inferior cerebellar artery supplies a highly localized area on the lateral side of the medulla and the adjacent cerebellum. As a result, the pathology and the clinical picture can be precisely correlated as is done in the article.

The patient suddenly experiences dizziness and headache, then tends to fall toward the side of the lesion. He cannot swallow and no longer can feel pain sensation on the homolateral side of his head and the contralateral side of his body below the head. The homolateral extremities are ataxic. The patient does not lose consciousness and there are no signs of pyramidal tract involvement.

The differential diagnosis, prognosis and treatment are briefly outlined. Summaries of three illustrative cases are included.

A. Pengelly

OPHTHALMOLOGY

Aneurysm of The Posterior Communicating Artery, B. J. Alpers, N. A. Schlezinger, Archives of Ophthalmology, **42:** 353-364 (Oct. 1949).

A group of cases of aneurysm of the posterior communicating artery is presented in order to call attention to salient features for diagnosis, as well as to indicate the possibilities of treatment.

The clinical history of recurrent headaches associated with the development of ophthalmoplegia involving the third nerve appears to be the most significant feature in the diagnosis. Little else has been found to be helpful except the arteriogram, the presence of retinal arteriosclerosis and x-ray evidence of calcification of the internal carotid arteries. In 4 of 6 cases, operation was successful. In the 7th case, death occurred before operation could be accomplished.

The spinal fluid is normal except in rare cases where syphilis is the cause and in the more frequent circumstances of rupture of the aneurysm where bloody or xanthochromic spinal fluid is found.

J. I. Leventhal

SURGERY

Observations on Experimental Aortic Anastomosis, F. Glenn, E. B. C. Keefer, C. T. Dolter, J. M. Beal, Proc. Soc. Exp. Biol. Med., **71:** 619-622 (Aug., 1949).

Congenital coarctation of the aorta consists of stenosis of the vessel at the approximate level of the entry of the ductus arteriosus in the foetal vascular system. About 74% of people so afflicted die at an average age of 30 years. Surgical intervention involves the excision of the malformed segment of the aorta with subsequent end to end anastomosis.

The authors subjected seven young dogs between 3 and 8 weeks old to division of the thoracic aorta and end to end anastomosis. All of the dogs survived and at the end of a year the site of operation was examined by angiocardiography and finally by removal of the site of anastomosis in one of them. Thus it was found that in all cases there was a definite narrowing of the lumen at the site of anastomosis as well as the expected scar tissue. The authors give two possible explanations for the stenosis: (1) the lumen at the site of the anastomosis did not keep pace in growth with the rest of the aorta; (2) a single continuous suture was used.

The results of the experiment indicate that surgical intervention for coarctation of the aorta in humans should be deferred until the lumen is large enough to ensure an adequate size as the individual grows to maturity. Experience with humans has shown that the operation should be delayed until the age of 6 to 8 years is attained. On the other hand the operation should take place relatively early prior to maturity because atheromatous changes in the aorta tend to occur early in association with this malformation.

S. Librach

Primary Pulmonary Malignancy. Ochsner et al: J. Thoracic Surg., **17**, 573-599 (Oct. 1948)

A summary of results in 548 cases of primary pulmonary malignancy is presented. Of these, 35.4% were found to be inoperable, 6% refused operation, 56.1% were subjected to exploratory thoracotomy and 35.6% of the total had resectable lesions. Thus of three patients with lung tumor, 1 is inoperable initially, 1 is found inoperable at operation and only 1 has a resectable lesion. In the resection group there was a hospital mortality rate of 16.4%, resulting from cardiovascular and respiratory disease complicated by haemorrhage. Of the resections carried out 70% were considered palliative and justifiably so, since the risk was not excessive, life was made more comfortable and the survival period was increased. The gross survival rate (palliative and curative) at the end of three years was 20%, with little change at five years. Of these, palliative cases had a 10% three-year survival rate, curative cases 35%. In the non-resection group, none was alive at the end of five years.

Miss A. I. Scott

UROLOGY

Etiology and Management of Renal Lithiasis. C. C. Higgins, J. Urology, **62:** 403-409, (Oct., 1949).

The author discusses the following factors in the aetiology of renal lithiasis:

1. Vitamin A deficiency
2. Hyperparathyroidism
3. Hypercalcinuria due to other factors, e.g., impaired renal function, high calcium and phosphorus intake in the diet, vitamin D, high acid ash diet
4. Infection in the urinary tract
5. Focal infection
6. Stasis
7. Metabolic diseases, e.g., Gout
8. Cystinuria—a familial disease in which cystine is present in the urine owing to derangement of intermediate protein metabolism
9. Oxaluria
10. Xanthinuria and excessive amounts of other purine bases of dietary origin
11. Phosphaturia.

The author advises conservative renal surgery in cases of renal lithiasis because of the high incidence of recurrence or formation of a stone in the opposite kidney, because infections of the urinary tract respond well to the chemotherapeutic agents now available, and because better techniques of pyelolithotomy and nephrolithotomy are being developed thus reducing the number of nephrectomies that need to be done.

Post operative management should include a large fluid intake and output, eradication of infection in the urinary tract, elimination of foci of infection and stasis, correction of metabolic disease if present, large amounts of vitamin A, exploration of parathyroid glands if there is evidence of their hyperactivity.

Dietary management is governed by the chemical constituents of the calculus, the crystals observed in the urine and the blood chemistry findings.

W. J. D. Cooke

NEWS AND NOTES

MEDICAL SOCIETY.

On February 15, the Medical Society will be sponsoring a new and distinctive Meds At-Home. The location, the Royal York Hotel, will be the same as other years, but that's about all. The floor space is expanded to include the Crystal Ballroom as well as the Concert Hall, and Mart Kenny and his Western Gentlemen will be one of two orchestras in attendance. Dress is optional, and arrangements have been completed for lounging facilities and refreshments. The decorations are to be in keeping with the International theme of the dance. Appropriate entertainment is being rehearsed by Faculty undergraduates. Much thought and effort has already gone into the planning of the dance; much will be done in the days ahead. With enthusiastic student support, the Meds At-Home will be the dance of the year!

* * *

Returns from the Faculty Undergraduate Campaign for the Hospital for Sick Children were encouraging. A total of $480 was contributed, Meds 5T2 and Premeds 5T4 made the largest donations. The Hospital was pleased with the response, and Mr. Laidlaw, Chairman of the Campaign, has been good enough to write the class Presidents individual letters.

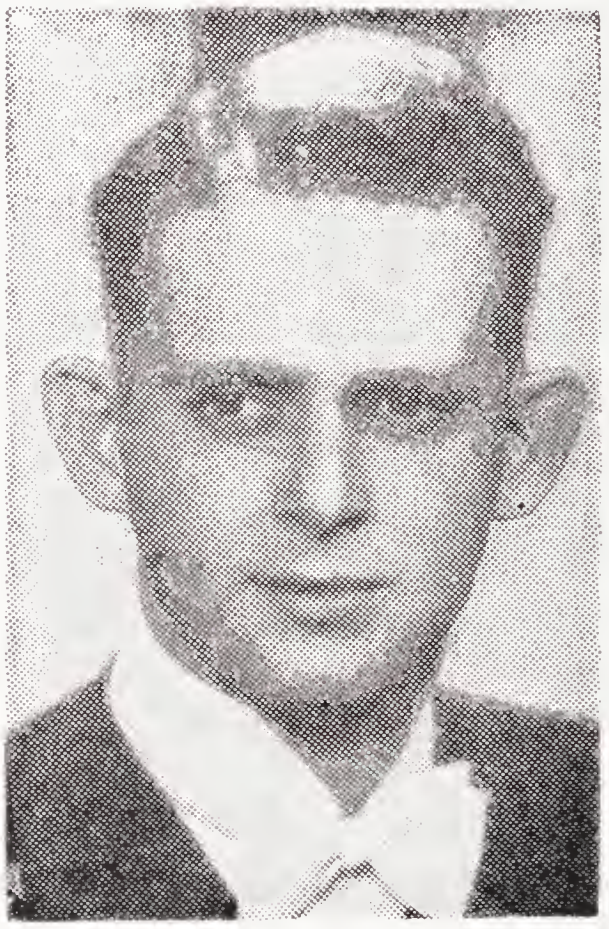
* * *

Eleven University of Toronto Medical Undergraduates have been recently honoured by election to the University Chapter, Alpha Omega Alpha, Honour Medical Fraternity. These include Mr. S. Bogoch, Mr. W. B. M. Hick, Mr. E. Klein, Mr. P. H. Melville, and Miss S. M. Ramcharan, of Meds 5T1; Mr. J. A. Beswick, Mr. R. M. Clark, Mrs. R. P. Field, Mr. D. B. McConachie, Mr. J. F. H. Stewart, and Mr. S. H. Witzel, of Meds 5T0.

* * *

Appointment of Mr. Robert Franklin Hetherington as Rhodes Scholar has been announced. Bob is a native of British Columbia. While at Oak Bay High School in Victoria, he was a member of school teams in rugby, football, basketball, soccer, lacrosse, and track and field. After one year in arts and sciences at the University of British Columbia, Bob joined the navy at 18. From Newfoundland, he did a three-month period of sea duty, and was awaiting officer training for duty in the Pacific when the Far East War ended. He was demobilized in 1945, and returned to the University of British Columbia where he completed a second year of arts.

At the University of Toronto, Bob has obtained first-class standing for three years, leading his



ROBERT F. HETHERINGTON

class in his first and third years. He was awarded the Posluns Brothers Scholarship in Anatomy, Physiology, and Biochemistry in 1948, and the Ronald S. Saddington Medal in Pathology in 1949. In October, 1948, he was elected a member of Alpha Omega Alpha.

At both Universities, Bob has been active in sports. At the University of British Columbia, he played senior basketball and rugby; at the University of Toronto, he has played Meds lacrosse and basketball. He also plays golf and tennis, swims, sails, and skis.

Last year, Bob was Vice-President of the Medical Society. This year he is President. In addition, he is President of the Students' Administrative Council of the University.

Bob's plans for the immediate future are still somewhat indefinite. He will enter Oxford in October, and expects to take a year of basic science before passing on to clinical work at the

Radcliffe Infirmary, or some other of the Oxford-associated hospitals.

* * *

Other scholarships have been announced recently. Mr. D. I. Gove, Meds 5T0, has received the Charles E. Frosst Scholarship, valued at $250, for his essay on "Advances in the Knowledge of Carbohydrate Metabolism". Medical Alumni Association Scholarships, of the value of $200 each, have been awarded to Mr. D. A. Smith, Meds 5T1; and to Mr. W. D. Friend, Meds 5T2. The William Edward Corlett Memorial Scholarship, tenable throughout the four years of the undergraduate medical course, has been awarded to Mr. R. O. Antoni, Meds 5T3. The Jay J. Allen Award has this year, for the first time since 1946, been won by a Medical student, Mr. M. Wasylenki, Meds 5T3.

* * *

The Medical Athletic Association announces that a Spring Athletic Dance will again be held this year, in conjunction with the Medical Society Elections.

FACULTY.

A successful refresher course in Ophthalmology and Oto-Laryngology has just been completed at the University School. The course began January 9, and ended January 14. The Hospital for Sick Children, and the Toronto Western Hospital, are holding a joint course for General Practitioners, from January 26 to January 28 inclusive.

* * *

Dr. C. H. Best has completed a two months' visit to South Africa, where he has lectured and collected further data in connection with his studies of choline and cirrhosis of the liver.

* * *

Dr. Clifford Ash has been awarded a fellowship by the Quebec division of the Canadian Cancer Society in connection with the British Empire Cancer Campaign.

ALUMNI.

Dr. J. G. Lamont, Meds 9T5, has been re-appointed for a two year term as Medical Director of the Grafton State School in North Dakota, a mental institution with 1200 patients. Dr. Maurice Snitman, Meds 2T6, has been promoted to the rank of Associate Professor of Otolaryngology at the University of Illinois College of Medicine. Dr. P. H. Starr, Meds 4T4, has been awarded a Washington University (St. Louis) Fellowship in neuropsychiatry.

ROBERT L. SMITH

WELCH ALLYN
OPHTHALMOSCOPE

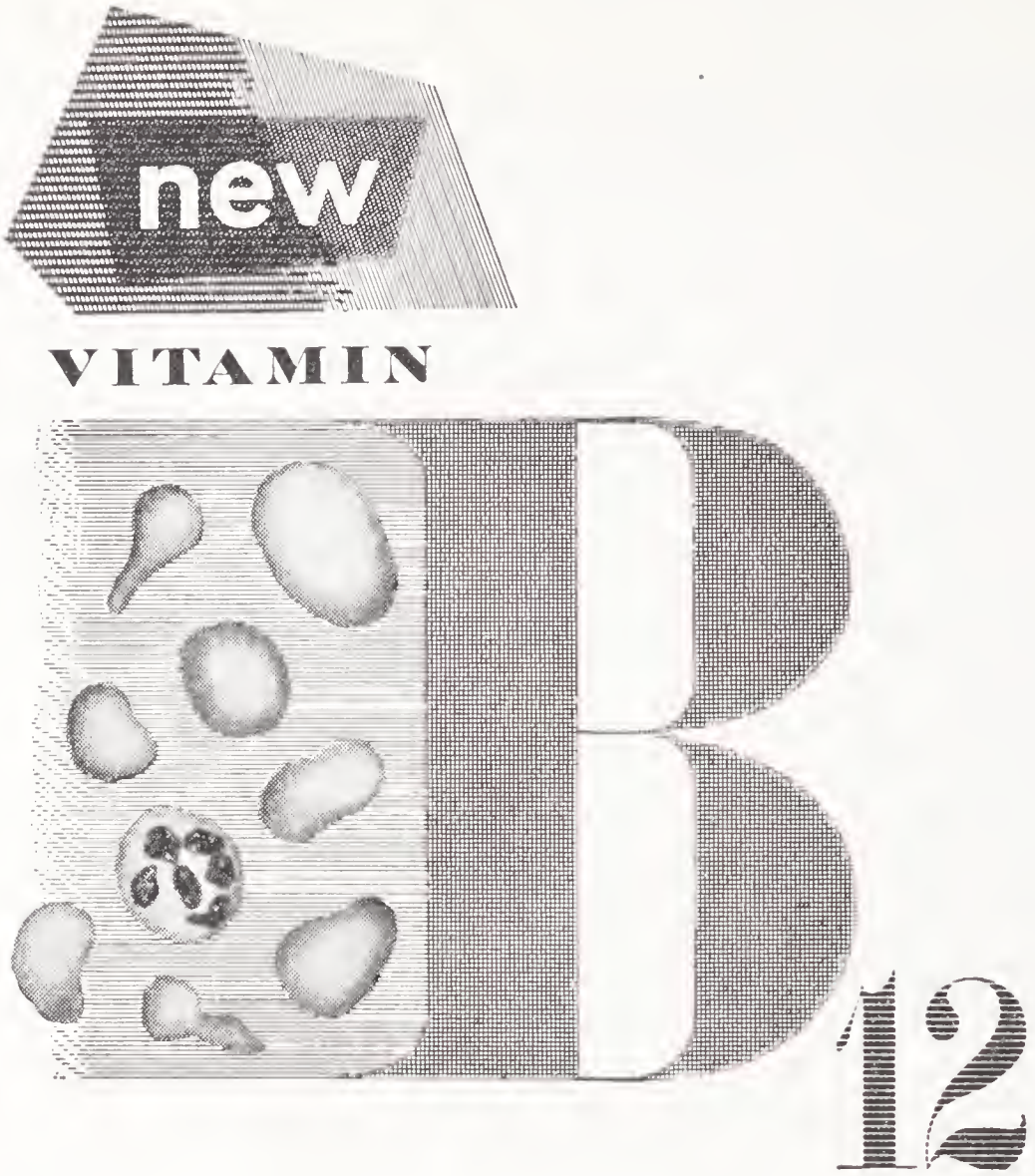
With Illuminating and Lens System as devised by Dr. C. H. May

In addition, has a Sliding Diaphragm Device giving

- SLIT APERTURE
- PIN HOLE APERTURE
- CLEAR APERTURE
- "WHITE LINE" GRID FILTER
- RED FREE FILTER

THE J. F. HARTZ CO. LIMITED

MONTREAL TORONTO HALIFAX



"Vitamin B_{12} per unit of weight, is the most effective antianemic substance known." SPIES ET AL.: J. A. M. A. 139: 521, 1949

RUBRAMIN

SQUIBB vitamin B_{12} concentrate.

now in plentiful supply

- ▶ essentially painless, protein-free aqueous solution
- ▶ approximately the same cost as Liver Extract

1 cc. ampuls, each ampul containing 15 micrograms of vitamin B_{12}. Boxes of 5.

5 cc. vials containing 30 micrograms of Vitamin B_{12} per cc.

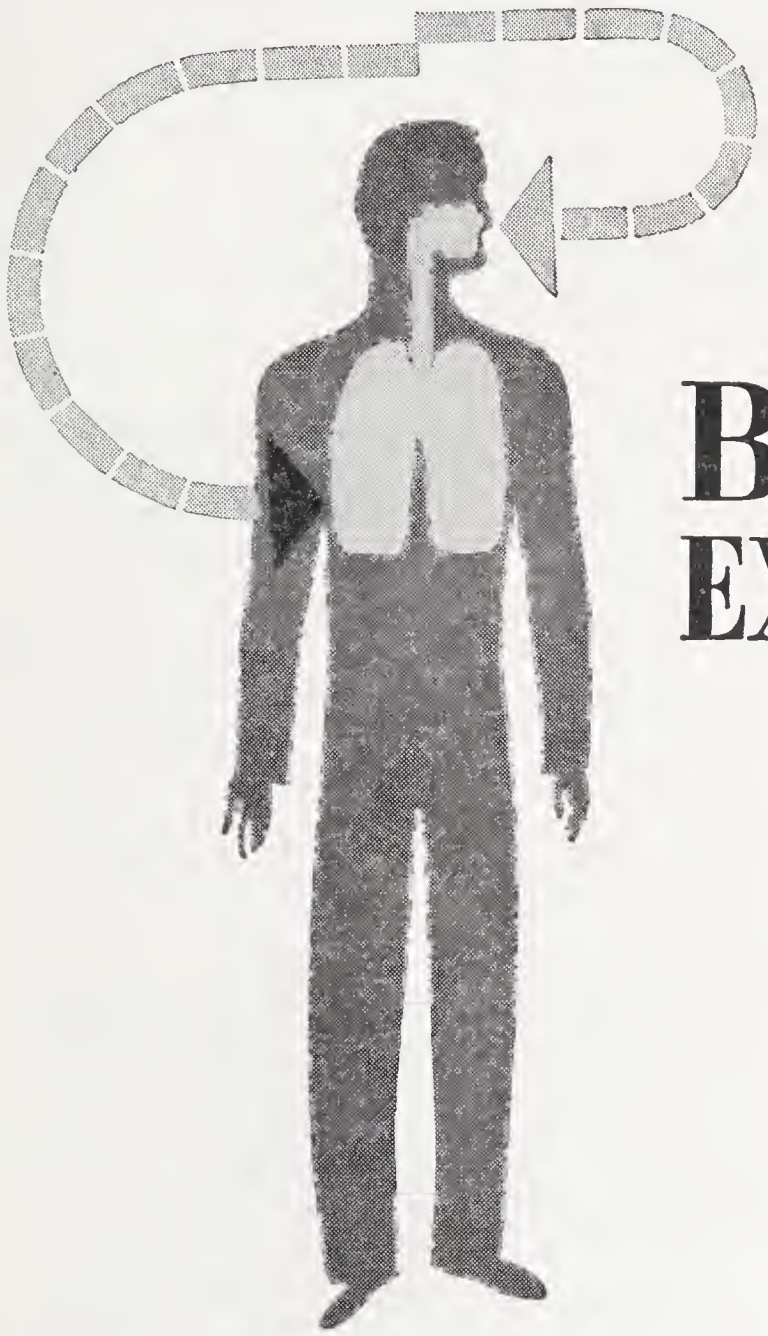
Dosage for 15 microgram RUBRAMIN is the same as that for 15 unit Liver Extract.

'RUBRAMIN' IS A TRADEMARK OF E. R. SQUIBB & SONS

E. R. SQUIBB & SONS OF CANADA, LIMITED,
2245 VIAU STREET, MONTREAL

SQUIBB MANUFACTURING CHEMISTS TO THE MEDICAL PROFESSION SINCE 1858

a completely new approach to cough relief



The antispasmodic and decongestant action of BENYLIN EXPECTORANT combats cough, relaxes the bronchial tree, diminishes bronchial congestion and alleviates nasal stuffiness, sneezing and lacrimation. Containing no narcotics, BENYLIN EXPECTORANT combines Benadryl® hydrochloride, 10 mg. per teaspoonful, with other remedial agents for safe, effective control of coughs due to colds as well as those of allergic origin.

BENYLIN® EXPECTORANT

promotes liquefaction and removal of mucous secretions from the respiratory tract. The demulcent action of its vehicle soothes irritated mucosa. Acceptable alike to children and adults, its pleasant, mildly tart taste avoids the objections to cloying, overly-sweet preparations.

DOSAGE: One or two teaspoonfuls every two to three hours, as soon as possible following appearance of symptoms. Children, ½ to one teaspoonful every three hours.

BENYLIN EXPECTORANT contains in each fluid ounce:

Benadryl Hydrochloride (diphenhydramine hydrochloride, P. D. & Co.)	80 mg.
Ammonium Chloride	12 gr.
Sodium Citrate	5 gr.
Chloroform	2 gr.
Menthol	1/10 gr.

BENYLIN EXPECTORANT is supplied in 16-oz., ½ and 1 gal. bottles.

PARKE, DAVIS & CO., LTD. • WALKERVILLE, ONTARIO

MEDICAMENTA VERA • P D & CO.

THE TREATMENT OF PINWORM INFESTATION

"VERMILET"
Tablets

Enteric coated tablets of Gentian Violet "Frosst"

Infestation with pinworms is common in children and not unknown in adults. The high incidence of infestation revealed in recent surveys makes this condition a major public health problem. Symptoms may be entirely absent. Diagnosis is best established by using The National Institute of Health technique of stroking the skin-anal margin with a cellophane swab in the morning before bathing, and examining the swab for ova of the parasite.

The demonstration of pinworms in one member of a family should render the entire family suspect, and all infested individuals should be treated simultaneously.

Fortunately, 90% of cases can be cured within a short time with little inconvenience. Clinical records show that the most effective treatment is the administration of gentian violet, in the form of tablets. "Vermilet" Tablets are specially made to pass undissolved through the stomach and to dissolve in the lower part of the ileum.

NOTE:—Gentian violet is contra-indicated in heart disease, hepatic and renal disease, gastro-enteritis, pregnancy, and in the presence of febrile or debilitating diseases.

DOSAGE

INFANTS:—Under three years of age, 3/20 gr. (9.6 mg.) for each apparent year of age. For children unable to swallow a tablet, it is suggested that the tablet be concealed in a teaspoonful of oatmeal; the child will swallow the tablet with a bolus of the cereal.

CHILDREN:—Over 3 years of age, 3/20 gr. (9.6 mg.) for each apparent year of age, divided in three parts and taken before meals. From 10 to 16 years of age, one tablet of ½ gr. (32 mg.) three times daily before meals.

ADULTS:—Two tablets of ½ gr. (32 mg.) three times daily before meals.

Repeat dose daily for 8 days, rest for one week, then repeat dose for additional 8 days. No patient should be discharged as cured unless 3 or 4 swabs, examined at intervals of a week apart, show absence of ova

"VERMILET"
Tablets

E.C.T. No. 409 "Frosst" 3/20 gr. (9.6 mg.)
E.C.T. No. 410 "Frosst" ½ gr. (32 mg.)

Bottles of 200 and 500 tablets.

A package of swabs and literature describing technique for demonstrating the ova will be sent free upon request.

Charles E. Frosst & Co.
MONTREAL CANADA

Poulenc Laboratories

have developed these products all of which are rapidly receiving the greatest commendation in Canada, France, Great Britain and the United States for their extreme originality and their donation to medical advancement

DIPARCOL
DILVASENE
NEO-ANTERGAN
PARSIDOL
FLAXEDIL
PHENERGAN

Samples and literature available upon request

POULENC
Limited

Montreal

COUNCIL ACCEPTED

For the Failing Heart of Middle Life
Prescribe 2 or 3 tablets of Theocalcin, t. i. d. After relief is obtained, continue with smaller doses to keep the patient comfortable. Theocalcin strengthens heart action, diminishes dyspnea and reduces edema.

Theocalcin, theobromine-calcium salicylate, T. M. Reg. Canada Product of Bilhuber Knoll Corp., Orange, N. J.

MERCK & CO. Ltd. Selling Agents **MONTREAL**

Flexible Formulas

with DEXTRI-MALTOSE

simple to prescribe...simple to prepare

Milk plus water plus Dextri-Maltose*—*simple to prescribe*—
is the mixture most widely used in the flexible formula system
of infant feeding. Dextri-Maltose has helped physicians
to build this system, now recognized the world over.

Formulas with Dextri-Maltose are *simple to prepare.*
Dextri-Maltose is easily
measured, is readily
soluble, and can be used
in any method of
formula preparation.

*Trademark Registered

Local Representative: J. D. Langlois, Jr.,
25 Kingsgarden Road, Toronto 10, Ontario, Canada, Lyndhurst 8055.

Facts for Quick Reference

"UROMAND"

"Frosst" brand of "Urosine" and Mandelate Compound

An improved URINARY ANTISEPTIC

Uromand has proven a very effective urinary antiseptic, its administration unattended by untoward effects which sometimes follow sulfonamide therapy. When Uromand is given in adequate dosage the pH of the urine reaches 5.0 to 5.3, at which level, especially in the presence of Urosine, many pathogenic organisms are unable to flourish and the urine becomes sterile.

"UROMAND"

C.T. No. 8 "Frosst"

Urosine (Brand of Hexamine).....	1¼ gr. (80 mg.)
Calcium mandelate.....	5 gr. (0.3 G.)
Ammonium acid phosphate.....	2½ gr. (0.16G.)

DOSAGE

8 to 20 tablets per day may need to be taken to provide full therapeutic effects. At least 8 glasses of water should be taken in the 24 hours to assure adequate diuresis.

MODES OF ISSUE

Bottles of 100 and 500 tablets.

Frosst
SINCE 1899
THE SYMBOL OF PROGRESS IN PHARMACEUTICAL RESEARCH

Charles E. Frosst & Co.
MONTREAL CANADA

Facts for Quick Reference

"SULFAMUL"

A non-hygroscopic, oil-in-water emulsion containing 5% sulfathiazole "Frosst"

For the treatment of:
**BURNS, INFECTED WOUNDS,
ABSCESS CAVITIES,
SUPERFICIAL SKIN INFECTIONS,
VAGINAL INFECTIONS.**

The most effective concentration . . . the most effective vehicle . . . the most effective method yet developed for local application of sulfathiazole. Sulfamul is applied with minimum discomfort to the patient, provides definite local anaesthetic action, requires no frequent changes of dressing, tends to shorten healing time and promotes most satisfactory cosmetic results.

ADMINISTRATION

Sterile gauze is impregnated with Sulfamul and then packed with moderate firmness into abscess or other infected cavity. The pack may be left in position for periods up to 72 hours, surface changes only being made. In superficial infections, Sulfamul or Sulfamul impregnated gauze may be directly applied.

MODES OF ISSUE

2 ounce, 1 pound and 7 pound glass jars.

"SULFAMUL" OPHTHALMIC

For the treatment of eye infections such as conjunctivitis and other pyogenic infections about the eyelids. Remarkable effects have been obtained where the emulsion has been applied locally.

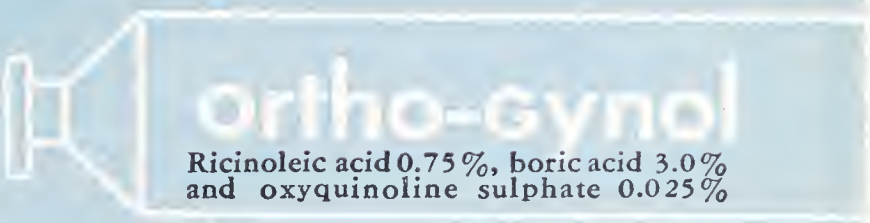
Available in 1/8 ounce, long-nozzle, collapsible tubes.

Frosst
SINCE 1899
THE SYMBOL OF PROGRESS IN PHARMACEUTICAL RESEARCH

Charles E. Frosst & Co.
MONTREAL CANADA

Simplicity

When the use of an occlusive diaphragm is not feasible anatomically, or is rejected by the patient, a simple method of high effectiveness is the intravaginal application of Ortho-Gynol vaginal jelly.[1] Deposited high in the vagina with the Ortho applicator, Ortho-Gynol, by its optimal viscosity, adhesiveness and surface tension, spreads uniformly as a clinging layer over the vaginal mucosa and cervix; thereby producing an effective barrier. Involving a minimum of manipulation, this dependable method is readily acceptable to patients for reasons of simplicity.



Ricinoleic acid 0.75%, boric acid 3.0% and oxyquinoline sulphate 0.025%

whenever indicated—wherever prescribed

Bibliography: 1. Ware, H. H. Jr.: Virginia M. Monthly 70:238, 1943

ortho

PHARMACEUTICAL CORPORATION (CANADA) LIMITED
TORONTO, ONT.

when pain strikes...

more and more physicians

are turning to

E.B.S. Methadon

This highly potent synthetic analgesic is replacing morphine in a multitude of uses. There are several reasons:

1 No withdrawal symptoms after therapeutic use.

2 No cumulative effect in ordinary courses of use.

3 Withdrawal syndrome after long use is very mild compared to that of other narcotics.

4 The hypnotic effect is slight, the action of Methadon E.B.S. being almost entirely analgesic in nature.

5 Methadon E.B.S. relieves some types of pain, such as renal colic, not controlled by opium derivatives.

note: To help avoid the confusion inherent in a multitude of proprietary names for single-drug products, the E. B. Shuttleworth Chemical Co. has adopted the policy of naming such products with their official names. Physicians are requested to co-operate in this effort by adding the letters E.B.S. to the product name when writing prescriptions. Thus:

℞ C.T. #452
Methadon
EBS., 5 mg.

AVAILABILITY:

C.T. # 452 Methadon E.B.S. 5 mg.
C. T. #453 Methadon E.B.S. 10 mg.
in bottles of 100, 500 or 1000.
H.T. Methadon E.B.S. 2.5 mg.
H.T. Methadon E.B.S. 5.0 m.g.
H.T. Methadon E.B.S. 10.0 m.g.
in bottles of 25 or 100.

Sterile Solution Methadon E.B.S.
No. A-86, 10 mg. per cc. in 30 cc. rubber capped vials.
No. A-87, 10 mg. per cc. in 1 cc. ampoules in boxes of 6 or 25.

THE E.B.S. SHUTTLEWORTH CHEMICAL CO. LTD., TORONTO, CANADA

AN ALL CANADIAN COMPANY . . . SINCE 1879

How Heinz safeguards the babies in your care

Heinz Baby Foods are dated to ensure fresh stocks

Every tin of Heinz Strained and Junior Foods carries a *code number*, showing the date it was packed—the day and the year. Heinz salesmen check these numbers when they make their frequent visits to grocers' and druggists' stores, to make certain that the supplies in stock are always fresh.

Heinz takes this *special precaution* in order to be doubly sure that infants will get foods of the fine fresh quality that is so important in baby diets.

This checking at the point of sale is the last of several steps Heinz takes—from the selection and cleansing of the raw materials, through to the Quality Control Laboratories —all aimed at inspiring confidence in its products among doctors, nurses and mothers.

Heinz Baby Foods

57

27 STRAINED FOODS, 17 JUNIOR FOODS, 2 BABY CEREALS

BARDONA CAPSULE

a new gastric sedative and antispasmodic

Will.

Pentobarbital is effective as a sedative in heightened nervous conditions which so frequently accompany gastric disturbances. The beneficial effects of the barbiturates in nausea and vomiting, as in seasickness, pregnancy, vertigo and migraine, are well known.

Belladonna with its chief alkaloids atropine and hyoscine, relieves spasm of pyloris and other sphincters and at the same time prevents excessive contractions of the stomach and intestines.

Each capsule contains:

Sodium Pentobarbital . . . . . ¼ grain

Powdered Extract Belladonna B.P. . ¼ grain

Available in bottles of 100, 500, 1,000.

ETHICAL PRODUCTS PHARMACEUTICAL

CHARLES R. WILL & COMPANY LIMITED

LONDON, CANADA